Extracorporeal Circulation as an Alternative to Open-Chest Cardiac Compression for Cardiac Resuscitation*

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Open-chest direct cardiac compression represents a more potent but highly invasive option for cardiac resuscitation when conventional techniques of closed-chest cardiac resuscitation fail after prolonged cardiac arrest. We postulated that venoarterial extracorporeal circulation might be a more effective intervention with less trauma. In the setting of human cardiac resuscitation, however, controlled studies would be limited by strategic constraints. Accordingly, the effectiveness of open-chest cardiac compression was compared with that of extracorporeal circulation after a 15-min interval of untreated ventricular fibrillation in a porcine model of cardiac arrest. Sixteen domestic pigs were randomized to resuscitation by either peripheral venoarterial extracorporeal circulation or open-chest direct cardiac compression. During resuscitation, epinephrine was continuously infused into the right atrium, and defibrillation was attempted by transthoracic countershock at 2-min intervals. Systemic blood flows averaged 195 ml·kg⁻¹·min⁻¹ with extracorporeal circulation. This contrasted with direct cardiac compression, in which flows averaged only 40 ml·kg⁻¹·min⁻¹. Coronary perfusion pressure, the major determinant of resuscitability on the basis of earlier studies, was correspondingly lower (94 vs 29 mm Hg). Extracorporeal circulation, in conjunction with transthoracic DC countershock and epinephrine, successfully reestablished spontaneous circulation in each of eight animals after 15 min of untreated ventricular fibrillation. This contrasted with the outcome after open-chest cardiac compression, in which spontaneous circulation was reestablished in only four of eight animals (p = .038). We conclude that extracorporeal circulation is a more effective alternative to direct cardiac compression for cardiac resuscitation after protracted cardiac arrest.

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Electrical countershock is the immediate treatment for ventricular fibrillation. When applied within less than 60 s, it typically restores spontaneous circulation without additional interventions. When the duration of cardiac arrest is more prolonged, the success of resuscitation is contingent on the capability of achieving threshold levels of coronary perfusion pressure and therefore myocardial blood flow. The coronary perfusion pressure itself is highly predictive of the success of resuscitation.4-7

Current methods of closed-chest cardiac resuscitation lose effectiveness for maintaining critical coronary perfusion pressures when the duration of cardiac arrest prior to attempted cardiac resuscitation increases to more than 8 min. Accordingly, the success of closed-chest compression methods after more protracted intervals exceeding 8 min is remote.10,11

Open-chest direct cardiac compression is a well-established option by which substantially greater cardiac output and coronary perfusion pressures may be achieved.12-14 The success of resuscitation under experimental conditions is consequently increased two- to threefold, contingent on the duration of cardiac arrest prior to open-chest cardiac massage.4,15,16 It is for these reasons that open-chest techniques have been investigated as an option when conventional methods of closed-chest resuscitation fail to restore spontaneous circulation.17,18 Yet the practical issues of surgical skill and postthoracotomy patient care, together with insecure proof of ultimate clinical benefit, have restrained the routine use of open-chest techniques.

More recent studies in animal models of cardiac arrest and reports on human victims of cardiac arrest have provided evidence that extracorporeal circulation (utilizing peripheral vascular access) may be a highly effective option for cardiac resuscitation.9,19-23 In our studies, extracorporeal circulation successfully restored spontaneous circulation in 19 of 21 pigs after a 15-min interval of cardiac arrest. This contrasted with closed-chest resuscitation, in which none of five animals was resuscitated.9
In the present studies, we compared the effectiveness of extracorporeal circulation and direct cardiac compression following 15 min of untreated cardiac arrest with the anticipation that extracorporeal circulation would be more effective for restoring spontaneous circulation.

Methods

The studies were approved by our University Animal Care Committee, and the procedures were performed in accord with National Institutes of Health guidelines.

Animal Preparation

Our previously described porcine model of cardiac arrest and the methods developed in our laboratory for resuscitation by extracorporeal circulation were utilized. In preliminary trials, the porcine model was also adapted for investigations of open-chest cardiac compression. A total of 16 randomized experiments were planned to investigate whether extracorporeal circulation was a more effective alternative to open-chest direct cardiac compression in eight animals each.

In brief, domestic pigs weighing between 22 and 31 kg were fasted for 12 h. Anesthesia was induced by intramuscular injection of ketamine (30 mg per kilogram of body weight), followed by intravenous injection of sodium pentobarbital (30 mg/kg). The trachea was intubated, and the lungs were ventilated with a volume-controlled ventilator at a frequency of 12 breaths per minute, tidal volume of 12 ml/kg, and FIO2 of 0.5. The respiratory rate was adjusted to maintain arterial PCO2 at 33 to 45 mm Hg. Anesthesia was maintained with intravenous doses of pentobarbital (8 mg/kg) at 30-min intervals. Neuromuscular blockade was induced by intravenous injection of pancuronium (0.08 mg/kg) and was maintained with supplemental doses (0.05 mg/kg) at intervals of 60 min.

For aortic pressure measurements and blood sampling, an 8F angiographic catheter was advanced from the left carotid artery into the ascending thoracic aorta. The left carotid artery was used because the femoral arteries were reserved for extracorporeal circulation. For measurements of cardiac output, core temperature, and right atrial pressures, a balloon-tipped pentalumen thermistor catheter was flow-directed from the right femoral vein into the pulmonary artery. The proximal port was used for continuous infusion of epinephrine into the right atrium during cardiac resuscitation. For coronary venous blood measurements, a 7F angiographic catheter was advanced from the left cephalic vein into the great cardiac vein with fluoroscopic guidance. For induction of ventricular fibrillation, a 4F pacing electrode was advanced from the right cephalic vein into the right ventricle such that its tip impinged on the right ventricular endocardium.

Prior to induction of cardiac arrest, the animals were randomized. Either vascular cannulation was performed in preparation for extracorporeal circulation, or thoracotomy was performed in preparation for open-chest cardiac compression.

For extracorporeal circulation, a centrifugal pump (model 7850 Sarns Inc, 3M, Ann Arbor, Mich) and a capillary membrane oxygenator (model BOS-CM40, American Bentley, Irvine, Calif) were connected in series utilizing Bentley Bypass TM70 tubing (American Bentley). Either the blood interface of the extracorporeal circuit was coated with heparin (four animals), or systemic anticoagulation was produced with bovine heparin in doses of 100 IU/kg injected into the venous circuit of the oxygenator immediately prior to induction of ventricular fibrillation (four animals). The dead space of the pump, oxygenator, and cannulas was filled with 6 percent hemostatic in 0.9 percent NaCl (Hespan, Du Pont Merck, Wilmington, Del). Extracorporeal nonpulsatile flow was maintained with a centrifugal pump (model 7800 Sarns Inc, 3M, Ann Arbor, Mich).

For venous access, a 17F multiple-hole, thin-walled cannula (C-PFBS-1600, Cook Inc, Bloomington, Ind) was advanced through the left external jugular vein into the superior vena cava. Under fluoroscopic visualization, the tip was positioned at the junction of the right atrium with the inferior vena cava. For arterial return (in pigs the femoral artery is of much smaller dimension than in humans or dogs), two 14F cannulas (William Harvey model 1836 USC1 C.B. Bart Inc, Billerica, Mass) were advanced from each of the femoral arteries into the external iliac arteries.

In preparation for internal cardiac massage, the skin, subcutaneous tissue, and muscles of the left fifth intercostal space were incised between the midclavicular line and the midaxillary line, and hemostasis was obtained with electrocautery. The parietal pleura was exposed and the rib cage was retracted for exposure of the heart. The parietal pericardium was incised in preparation for manual cardiac compression. The thoracic opening was then closed with the aid of clamps and reopened only immediately prior to cardiac compression. Aseptic techniques were used throughout the experiments.

Measurements

Cardiac output was measured during spontaneous circulation and during open-chest cardiac compression by thermolimitation technique with the aid of a cardiac output computer (model 9550, Baxter Edwards Laboratories) after bolus injection of 5 ml of 5 percent glucose at a temperature between 0°C and 4°C in the right atrium.

Extracorporeal flow was measured with an ultrasonic flow meter in the effluent tubing of the oxygenator (model T101, Transonic System Inc, Ithaca, N.Y.). Intravascular pressures were measured with fluid-filled catheters utilizing Statham P50 or P23db transducers (Spectramed, Oxnard, Calif).

Coronary perfusion pressure was calculated as the arithmetic difference between the end-diastolic aortic pressure and the time-coincident right atrial pressures during spontaneous circulation and during cardiac compression. In the absence of pulsatile aortic pressure during extracorporeal circulation, the difference between mean aortic and mean right atrial pressures served as estimate of coronary perfusion pressure. A scalar lead 2 ECG was recorded continuously.

Aortic and great cardiac vein blood gas values and pH were measured with a blood gas analyzer (model IL313, Instrumentation Labs, Lexington, Mass). Total hemoglobin and oxyhemoglobin were measured with a CO-oximeter (model IL282, Instrumentation Labs) with corrections for porcine blood. Oxygen content was calculated from the measured total hemoglobin, oxygen saturation, and PO2, utilizing an oxygen hemoglobin binding coefficient of 1.39 ml/g. Myocardial oxygen extraction was computed as the difference between arterial and coronary vein oxygen content divided by the arterial oxygen content.

Experimental Procedure

Prior to induction of cardiac arrest, the intravascular volume was expanded by administration of 6 percent hetastarch so as to increase pulmonary wedge pressure to 8 mm Hg. Core (pulmonary artery) temperature prior to cardiac arrest was maintained between 36.1°C and 37.1°C.

Ventricular fibrillation was induced by a 10-mA AC current delivered to the right ventricular endocardium and was confirmed by ECG morphology and coincident decrease in both mean aortic pressure and end-tidal PCO2. The inspired oxygen concentration was then increased to 100 percent. After 14 min 45 s of untreated ventricular fibrillation, a maximum of two 300-J transthoracic countershocks were delivered, which failed to reestablish spontaneous circulation in each instance. Either extracorporeal circulation or direct cardiac compression was then begun.

Extracorporeal flow was established at 200 ml/kg · min-1 and adjusted over the range of 161 to 285 ml/kg · min-1 contingent on venous return. The oxygen flow through the oxygenator was adjusted.
**Table 1—Outcome of Initial Defibrillation Attempts after 15 min of Untreated Ventricular Fibrillation**

<table>
<thead>
<tr>
<th>ECC (n = 8)</th>
<th>OCCC (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMD</td>
<td>7</td>
</tr>
<tr>
<td>Asystole</td>
<td>1</td>
</tr>
<tr>
<td>Ventricular fibrillation</td>
<td>0</td>
</tr>
</tbody>
</table>

*ECC = extracorporeal circulation; OCCC = open-chest cardiac compression; EMD = electromechanical dissociation.*

To maintain an oxygen-blood flow ratio of 2:1 to secure physiologic gas exchange. During cardiac compression, the heart was compressed against the sternum with the supinated palm with fingers extended. The rate was maintained between 60 and 80 per minute with equal compression and relaxation intervals. The operator was relieved at 5-min intervals. In preliminary trials in four animals, we confirmed that this method yielded greater cardiac output and mean aortic pressure with lesser trauma than compression between thumb and fingers.

Concurrently with the initiation of either extracorporeal circulation or direct cardiac compression, epinephrine hydrochloride (International Medication Systems Ltd, South El Monte, Calif) was infused into the right atrium in amounts of 3 μg·kg⁻¹·min⁻¹. In earlier studies with extracorporeal circulation, this favored restoration of spontaneous circulation within as little as 3 min. Defibrillation was attempted at 2-min intervals with up to two 300-J transthoracic countershocks. Successful resuscitation with return of spontaneous circulation was defined as a supraventricular rhythm and a spontaneous mean aortic pressure of 60 mm Hg. Failing such, resuscitation attempts were abandoned at 30 min after the start of the resuscitation procedures. The infusion of epinephrine was reduced by 25 percent decrements when spontaneously generated mean aortic pressure exceeded 65 mm Hg and was discontinued within an interval of 42 to 291 min (mean, 117 min).

**Statistical Analysis**

Data are presented as mean ± SD unless otherwise stated. The one-sided Fisher exact test was utilized to confirm or reject the hypothesis that extracorporeal circulation was more effective for cardiac resuscitation than open-chest precordial compression. A two-sided unpaired t test was utilized to compare differences for continuous data between extracorporeal circulation and open-chest cardiac compression. A p value less than 0.05 was regarded as significant.

**Results**

**Resuscitation**

Defibrillation failed to convert ventricular fibrillation in only two instances at the end of 15 min of untreated ventricular fibrillation. Most animals developed either electromechanical dissociation or asystole (Table 1). Within 2 min after the start of extracorporeal circulation or direct cardiac compression, electromechanical dissociation and asystole reverted to ventricular fibrillation in each instance.

With extracorporeal circulation, a supraventricular rhythm was restored in each instance within 5 min. Spontaneous circulation returned within an average of 7.3 min (range, 3 to 25 min). With direct cardiac compression, spontaneous circulation was reestablished in only four of the eight animals within an average interval of 6.9 min (range, 3 to 11 min). In the remaining four animals, defibrillation resulted in either electromechanical dissociation or asystole, which persisted for 30 min. Thus, extracorporeal circulation in conjunction with epinephrine and DC countershock successfully restored spontaneous circulation in each of eight animals, compared with only four of eight animals that underwent open-chest cardiac compression (p = 0.038).

**Hemodynamic Effects**

The systemic blood flow generated by the extracorporeal system averaged 198 ± 11 ml·kg⁻¹·min⁻¹ and corresponded to 113 percent of prearrest cardiac output. With direct cardiac compression, cardiac output averaged 40 ± 4 ml·kg⁻¹·min⁻¹ (p = 0.0001); this

**Figure 1.** Greater mean aortic pressures (MAP) and coronary perfusion pressures (CPP) were produced by extracorporeal circulation (ECC) than by open-chest cardiac compression (OCCC). Significantly greater increases in end-tidal PaCO₂ (PetCO₂) were observed with direct cardiac compression. Values are shown as mean (circles) and standard error of the mean. VF = ventricular fibrillation; DF = defibrillation by DC countershock; # = p ≤ 0.01 and * = p ≤ 0.001 for ECC vs OCCC by unpaired t test.
corresponded to 27 percent of the prearrest level. The mean aortic and coronary perfusion pressures were correspondingly greater during extracorporeal circulation (Fig 1). The coronary perfusion pressure had increased to 76±39 mm Hg within 1 min and had reached 94±25 mm Hg by the third minute. With direct cardiac compression, the coronary perfusion pressure increased from 20±7 to 29±6 mm Hg (p=0.0001) during the initial 3-min interval. The amounts of epinephrine that were administered during direct cardiac compression exceeded those employed during extracorporeal circulation (4.8±1.5 vs 2.6±1.1 µg·kg⁻¹·min⁻¹, p=0.005).

During direct cardiac compression, end-tidal Pco₂ correlated with the cardiac output, as previously reported. After restoration of spontaneous circulation, PetCO₂ in four animals returned to prearrest levels (Fig 1). However, there was no significant correlation between PetCO₂ and cardiac output during extracorporeal circulation. This was consistent with prior observations, which indicated a linear relationship between pulmonary blood flow and PetCO₂ during closed and open-chest cardiac compression. Accordingly, there was insignificant pulmonary blood flow during extracorporeal circulation and prior to the return of spontaneous circulation.

**Gas Exchange and Metabolic Effects**

During ventricular fibrillation, profound acidemia with threefold increases in Pco₂ was demonstrated in great cardiac vein blood (Table 2). In arterial blood, however, concurrent alkalemia with decreases in PaCO₂ to one third of normal was documented. These changes were comparable to those previously reported by us in the porcine model. Two minutes after the start of extracorporeal circulation or direct cardiac compression, aortic Pco₂ increased to approximately 50 mm Hg and pH decreased to approximately 7.20 (H⁺ = 63 nmol/L). Coroanary vein acidemia and hypercarbia were rapidly reversed by extracorporeal circulation; this coincided with threefold increases in great cardiac vein oxygen content. With direct cardiac compression, however, the great cardiac vein acidaemia, hypercarbia, and oxygenation remained unchanged. Accordingly, the venoarterial gradients for H⁺ and Pco₂ and the myocardial oxygen extraction were reduced only by extracorporeal circulation (Fig 2).

The hemodynamic and gas exchange measurements in animals that were successfully resuscitated by direct cardiac compression were then compared with those in animals that were not successfully resuscitated after direct cardiac compression. We observed greater car-

| Table 2—Aortic and Coronary Vein Values before, during, and after Attempted Resuscitation by Extracorporeal Circulation and by Open-Chest Cardiac Compression* |
|----------------------------------|------------------|------------------|------------------|------------------|
|                                  | Prearrest         | VF               | Resuscitation    | Postresuscitation |
|                                  | −5 min            | +12 min          | +2 min           | +60 min           | +180 min         |
| **P**<sub>O</sub>, mm Hg        |                  |                  |                  |                  |
| ECC Ao                           | 231±36            | 259±99           | 113±56           | 403±34            | 393±40           |
| ECC CV                           | 20±2              | 40±11(3)         | 54±10            | 50±16             | 34±15            |
| OCCC Ao                          | 210±31            | 240±100          | 66±26            | 314±112           | 356±84           |
| OCCC CV                          | 23±3†             | 35±8(4)          | 34±13‡           | 54±11             | 37±10            |
| **O**<sub>2</sub>, volume %     |                  |                  |                  |                  |
| ECC Ao                           | 10.2±1.8          | 10.1±2.7         | 9.3±2.5          | 11.6±1.9          | 10.7±2.0         |
| ECC CV                           | 1.9±0.7           | 2.2±1.5(3)       | 6.6±1.7          | 6.4±2.9           | 3.8±2.8          |
| OCCC Ao                          | 10.1±1.3          | 9.7±2.3          | 10.3±3.0         | 15.0±3.9          | 14.6±2.9†        |
| OCCC CV                          | 2.3±0.5           | 2.7±1.0(4)       | 2.4±1.5§         | 9.4±2.8           | 5.1±2.1          |
| **P**<sub>CO</sub>₂, mm Hg      |                  |                  |                  |                  |
| ECC Ao                           | 40±4              | 14±7             | 49±6             | 46±4              | 39±5             |
| ECC CV                           | 50±5              | 155±36(3)        | 67±32            | 54±7              | 51±4             |
| OCCC Ao                          | 41±5              | 16±8             | 56±10            | 50±9              | 43±5             |
| OCCC CV                          | 49±7              | 150±93(4)        | 158±54‡          | 56±8              | 54±2             |
| **pH**                           |                  |                  |                  |                  |
| ECC Ao                           | 7.47±0.05         | 7.87±0.18        | 7.20±0.06        | 7.24±0.05         | 7.39±0.08        |
| ECC CV                           | 7.39±0.04         | 6.56±0.19(3)     | 7.06±0.20        | 7.20±0.04         | 7.31±0.06        |
| OCCC Ao                          | 7.48±0.05         | 7.82±0.12        | 7.25±0.05        | 7.21±0.07         | 7.32±0.05        |
| OCCC CV                          | 7.40±0.03         | 6.77±0.30(4)     | 6.76±0.17‡       | 7.18±0.07         | 7.25±0.03        |

*VF = ventricular fibrillation; ECC = extracorporeal circulation; Ao = aortic; CV = coronary vein; OCCC = open-chest cardiac compression.

Values are expressed as mean ± standard deviation. Values were obtained in eight animals except for postresuscitation OCCC (n = 4). Values in parentheses are number of samples obtained during VF.

†OCCC vs ECC, p<0.05.
‡OCCC vs ECC, p<0.01.
§OCCC vs ECC, p<0.001.
diac index and $P_{ETCO_2}$ and a lower myocardial oxygen extraction ratio (Table 3). However, differences in resuscitability were not explained by differences in coronary perfusion pressures in the setting of open-chest cardiac massage.

**Discussion**

These studies confirm previous investigations in both animals and human patients on the efficacy of extracorporeal circulation for cardiac resuscitation after prolonged arrest. Extracorporeal circulation sustained quantitatively normal systemic blood flows and served to "jump start" the heart within as little as 3 min.

With direct cardiac compression, however, cardiac output was only one fifth and coronary perfusion pressure only one third of that generated by extracorporeal circulation, notwithstanding optimal compression technique and larger doses of epinephrine. This is in contrast to the near-normal outputs and coronary perfusion pressures that are generated when open-chest cardiac compression is initiated within less than 3 min. This is consistent with previous observations on the hemodynamic effects of closed and open-chest cardiac compression with increasing duration of cardiac arrest. In a canine model, Sanders et al. reported a decrease in the coronary perfusion pressure generated by direct cardiac compression from 59 to 39 mm Hg when the preceding interval of cardiac arrest, which included closed-chest compression, was increased from 15 to 25 min. Accordingly, the low flows and pressures observed in the current model are best explained by the prolonged downtime prior to intervention.

Increasing downtime may also compromise resuscitability by increasing the minimal coronary perfusion pressure threshold required for successful resuscitation. When the duration of untreated ventricular fibrillation was increased from 9 to 15 min in our rodent model of cardiac arrest, resuscitability was correspondingly decreased even though coronary perfusion pressure was maintained at comparable levels. This may explain why only 50 percent of animals were successfully resuscitated by direct cardiac compres-

![Figure 2](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21661/)
sion even though coronary perfusion pressure exceeded by threefold the threshold levels that have been documented when resuscitation is initiated within 5 min. Accordingly, open-chest compression, like closed-chest cardiac compression, loses hemodynamic efficacy after prolonged cardiac arrest. Under these conditions, extracorporeal circulation emerges as a more effective option than open-chest cardiac compression. The clinical implications, however, pertain more specifically to witnessed cardiac arrest with prolonged downtime, especially so in the out-of-hospital setting.

Increases in coronary vein Pco2 serve as a sensitive indicator of global myocardial ischemia. Extracorporeal circulation rapidly decreased coronary vein hypercarbic acidosis with concurrent and striking increases in coronary vein oxygen tension. With direct cardiac compression, the more favorable outcomes were observed in animals with greater cardiac output and smaller myocardial oxygen extraction.

The experimental method was planned to secure uniformity of procedures and timing. Accordingly, vascular catheterization and thoracotomy were performed prior to initiation of cardiac arrest, and the studies were performed in pentobarbital-anesthetized animals. These conditions do not directly correspond to those that prevail in clinical settings of cardiac resuscitation. However, the results confirm that extracorporeal circulation is hemodynamically more effective than open-chest direct cardiac compression after prolonged cardiac arrest. It more promptly restores myocardial oxygenation, reverses hypercarbia, and consequently restores spontaneous circulation.

These studies did not address ultimate survival and cerebral resuscitability. Earlier reports, however, provide evidence of satisfactory recovery of brain function. Accordingly, extracorporeal circulation is likely to emerge as a more effective alternative to direct cardiac compression after protracted cardiac arrest. This notwithstanding, open-chest direct cardiac compression remains an effective intervention, especially under conditions when closed-chest techniques prove to be ineffective. This has become a practical issue with the emergence of PttCO2 measurements as an objective measurement of hemodynamic effectiveness of resuscitation procedures, as demonstrated in this study (Table 3) and in human victims of cardiac arrest.

References

3 Winkle RA, Medd H, Roden MA, Smith NA, Buch WS, Cardianni VA. Effect of duration of ventricular fibrillation on defibrillation
10 Eisenberg MS, Hallstrom AP, Copass MK, Berger L, Short F, Pierce J. Treatment of ventricular fibrillation: emergency medical technician defibrillation and paramedic services. JAMA 1984; 251:1723-26
12 Del Guercio LRM, Feins NR, Cohn JD, Comoraraswamy RP, Wollman SB, State D. Comparison of blood flow during external and internal cardiac massage in man. Circulation 1965; 31(suppl 1):1171-80
18 Standards and guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiac care (ECC). JAMA 1986; 255:2843-999
22 Beichman R, Joyo CI, Dembtsky WP, Griffith LD, Adamson