Augmented Efficacy of External CPR by Intermittent Occlusion of the Ascending Aorta

Wanchun Tang, MD; Max Harry Weil, MD, PhD; Marko Noc, MD; Shijie Sun, MD; Raül J. Gazmuri, MD; Joe Bisera, MSEE

Background. After prolonged cardiac arrest, conventional methods of closed-chest cardiac compression are ineffective. This is primarily because of failure to generate minimal threshold levels of coronary perfusion pressure for cardiac resuscitation. This report introduces a new option for cardiac resuscitation by use of a combination of intermittent ascending aortic balloon occlusion, aortic infusion, and precordial compression to increase the pressure gradient for coronary perfusion.

Methods and Results. Twenty anesthetized, mechanically ventilated, normovolemic domestic pigs were investigated. A 10F balloon catheter was advanced from the left femoral artery into the ascending aorta. Ventricular fibrillation was induced with an AC current delivered through an electrode catheter advanced into the right ventricle. Precordial compression was initiated after 7 minutes of untreated ventricular fibrillation. The animals were randomized to one of four groups: (1) balloon occlusion with proximal infusion of oxygenated saline, (2) balloon occlusion alone, (3) proximal aortic infusion together with epinephrine without balloon occlusion, and (4) injection of epinephrine without balloon occlusion or proximal infusion. For balloon occlusion, the balloon was inflated for 30 seconds during each minute of cardiopulmonary resuscitation. In the subsets of animals that received infusions, oxygenated saline (30 mL) was injected into the proximal aorta immediately after balloon occlusion. Epinephrine was used in two subsets: It was injected as a bolus in amounts of 30 μg/kg into the right atrium at 30 seconds after start of precordial compression and repeated as required to maintain coronary perfusion pressure within the range of 25 to 30 mm Hg. Defibrillation was attempted at 1 minute after start of precordial compression and at 1-minute intervals thereafter. Resuscitation attempts were continued until there was return of spontaneous circulation or for a total of 30 minutes after start of precordial compression. Coronary perfusion pressure generated by precordial compression was significantly increased after balloon occlusion. Each of 10 animals was successfully resuscitated and survived for 48 hours after balloon occlusion whether or not it was combined with infusion. Three of five animals were resuscitated by a combination of infusion and epinephrine in the absence of aortic occlusion, but none survived for 48 hours (P=.02). Only one epinephrine-treated animal was successfully resuscitated and survived for 48 hours in the absence of balloon occlusion or infusion (P<.05).

Conclusions. Ascending aortic balloon occlusion with or without proximal aortic infusion strikingly increased resuscitability and 48-hour survival after cardiac arrest under conditions when conventional methods failed. (Circulation. 1993;88[part 1]:1916-1921.)

Key Words: epinephrine • cardiopulmonary resuscitation • balloons • fibrillation • perfusion

During cardiac arrest, myocardial ischemia prompts maximal coronary blood flow such that myocardial blood flow becomes essentially pressure dependent.1-3 Although coronary blood flow may be reduced by the mechanical effects of ventricular fibrillation (VF) and by decreases in myocardial compliance and specifically the increased myocardial “stiffness” associated with ischemia, myocardial blood flow is remarkably well correlated with the pressure gradient between the aorta and right atrium during compression diastole, ie, the coronary perfusion pressure.4-7 Increases in coronary perfusion pressure therefore account for proportional increases in myocardial blood flow and resuscitability.8,9 Unfortunately, optimal techniques of closed-chest cardiac resuscitation generate cardiac outputs that approximate less than 25% and myocardial blood flow of only 33% of such resting values.3,5,9,10 Even maximal endogenous sympathoadrenal response and its accompanying arterial vasoconstriction may fail to increase coronary perfusion pressure to minimal thresholds necessary for restoring or sustaining myocardial viability.4,11

These limitations in current conventional techniques of cardiopulmonary resuscitation (CPR) have prompted the search for adjunctive and alternative methods by which coronary and therefore myocardial perfusion may be increased. Our initial studies were undertaken in an established model of VF in intact Sprague-Dawley...
rats.12 When boluses of oxygenated donor blood were injected from the carotid artery into the proximal aorta, defibrillation successfully restored spontaneous circulation.13 Neither precordial compression nor open-chest cardiac compression were used. However, the relatively large volumes of blood needed for successful resuscitation were likely to restrain its practical use in a clinical setting. These observations directed our attention to proximal aortic infusion combined with mechanical balloon obstruction to more distal aortic runoff as options for cardiac resuscitation when conventional techniques fail. Our hypothesis was that intermittent balloon occlusion of the ascending aorta, especially when combined with infusion of oxygen carrying fluid into the proximal aorta, would strikingly increase the effectiveness of precordial compression. Our intent was to improve resuscitability without compromise to postresuscitation survival and cerebral viability. The present studies were therefore performed to investigate the concept and technique of ascending aortic balloon occlusion as a new option for cardiac resuscitation using an established porcine model of cardiac resuscitation.10,14,15

**Methods**

**Experimental Design**

Four subsets of experiments were performed. For the purpose of defining the contribution of components of the combined interventions, the effects of balloon occlusion with proximal aortic infusion (group 1) and balloon occlusion alone (group 2) were separately examined. Epinephrine effectively increases aortic pressure and cardiac resuscitability and therefore is routinely used in conjunction with conventional closed-chest resuscitation.6,16 Accordingly, the balloon technique was also controlled against an animal model of conventional cardiac resuscitation in which precordial compression was combined with the administration of epinephrine in doses that were previously shown to favor maximal resuscitability.11,17 Accordingly, the effects of epinephrine with proximal aortic infusion (group 3) and epinephrine alone (group 4) without aortic occlusion were also separately examined.

**Procedures**

All animals received humane care in compliance with the *Principles of Laboratory Animal Care* formulated by the National Society for Medical Research and the *Guide for the Care and Use of Laboratory Animals* prepared by the Institute of Laboratory Animal Resources and published by the National Institutes of Health (NIH Publication 86-33, revised 1985).

Twenty domestic pigs weighing 38 to 45 kg were investigated. The animals were fasted overnight except for free access to water. Anesthesia was initiated by intramuscular injection of ketamine in a dose of 20 mg/kg and completed by ear vein injection of sodium pentobarbital in a dose of 30 mg/kg. After tracheal intubation, the animals were ventilated with a tidal volume of 15 mL/kg, peak flow of 40 L/min, and FIO2 of 0.5. Respiratory frequency was adjusted to maintain Paco2 between 35 and 40 mm Hg. End-tidal CO2 was monitored with an infrared analyzer (model 601 POET, Crit Care System, Milwaukee, Wis). Anesthesia was maintained with 8 mg/kg intravenous injections of pentobarbital at 30-minute intervals. Neuromuscular blockade was induced by intravenous injection of pancuronium bromide (0.1 mg/kg) and maintained by supplements of 0.05 mg/kg at 60-minute intervals. For measurements of pulmonary artery pressure, right atrial pressure, and blood temperature, a balloon-tipped pentalumen thermocatheter was flow directed from the right femoral vein into the pulmonary artery. For measurement of the distal aortic pressure, an 8F angiographic catheter was advanced from the right femoral artery into the descending thoracic aorta. For induction of ventricular fibrillation, a 4F pacing electrode was advanced from the right cephalic vein into the right ventricle with ECG monitoring such that its tip impinged on the right ventricular endocardium. A 10F balloon catheter (DRB, Datascop Corp, Oakland, NJ) with a distal port that allowed for both fluid infusion and measurement of proximal aortic pressure was advanced from the left femoral artery into the ascending aorta. The tip of the catheter was advanced to a site 3 to 5 cm distal to the aortic valve so that inflation of the balloon occluded the aorta between the aortic valve and the right brachiocephalic trunk. All catheter positions were confirmed by fluoroscopy and either characteristic pressure pulse morphology or endocardiogram. Blood temperature was continuously monitored in the pulmonary artery and maintained at 37.5 ± 0.5°C, using infrared surface heating as required. Aseptic techniques were used throughout the experiments.

**Measurements**

Dynamic data, including lead II ECG, intravascular pressure, end-tidal Pco2, tidal volume, and blood temperature, were recorded on a conventional 16-channel thermal recorder (model MT95000, Astro-Med Inc, West Warwick, RI) together with a PC-based data acquisition system supported by CODAS software. The coronary perfusion pressure was digitally computed in real time as the difference between the diastolic aortic and simultaneously measured right atrial pressure as previously described.10,14,15 The quantitative neurological deficit scores proposed by Bircher and Safar18 were used. The scale was based on observation of activity and neurological examination and estimated as percentage deficit. The percentage neurological deficit ranges from 0% (no deficit) to 100% (brain death).

**Experimental Procedure**

The animals were randomized immediately before inducing VF to one of the four groups as shown in the Table. VF was induced by a 5-mA alternating current delivered to the right ventricular endocardium. FIo2 was increased to 1.0. After 7 minutes of untreated VF, sternal compression was begun with a pneumatic piston device (Thumper, model 1000, Michigan Instruments, Grand Rapids, Mich). The chest was compressed at a rate of 100 min-1. The compression/ventilation ratio was 6:1 with equal compression-relaxation intervals. The aorta and right atrial pressures together with the differences between these pressures, ie, the coronary perfusion pressure, were digitally displayed. The force of compression was adjusted to decrease the anterior-posterior diameter of the chest by 25% to 30%. The proximal aortic balloon was inflated for an interval of 30 seconds of each minute, so that systemic, including
Differences in Resuscitability, Survival, and Neurological Outcome Among the Four Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Resuscitation</th>
<th>48-Hour Survival</th>
<th>24-Hour NDS</th>
<th>48-Hour NDS</th>
<th>CPR Duration, min</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Balloon occlusion with proximal infusion</td>
<td>5/5</td>
<td>5/5</td>
<td>11±2</td>
<td>3±2</td>
<td>16±4</td>
</tr>
<tr>
<td>2. Balloon occlusion without infusion</td>
<td>5/5</td>
<td>5/5</td>
<td>14±3</td>
<td>11±4†</td>
<td>14±3</td>
</tr>
<tr>
<td>3. No balloon occlusion, proximal infusion and epinephrine</td>
<td>3/5</td>
<td>0/5*</td>
<td>...</td>
<td>...</td>
<td>18±6</td>
</tr>
<tr>
<td>4. No balloon occlusion, no proximal infusion, epinephrine only</td>
<td>1/5*</td>
<td>1/5*</td>
<td>24</td>
<td>24</td>
<td>15</td>
</tr>
</tbody>
</table>

NDS indicates neurological deficit score; CPR, cardiopulmonary resuscitation.
*P<.05 vs 1 and 2; †P<.05 vs 1.

cerebral, perfusion would be maintained during this 30-second interval. Complete occlusion of the aorta was verified by an immediate increase in compression diastolic aortic pressure and corresponding increases in coronary perfusion pressure to levels exceeding 50 mm Hg (Fig 1). Physiological salt solution was equilibrated with gaseous oxygen to yield a Po2 exceeding 500 mm Hg. Thirty milliliters of the solution was injected over a 10-second interval immediately after balloon inflation. Defibrillation was attempted at 60-second intervals and immediately before balloon deflation. A single 300-J DC countershock was delivered between the second right interspace and the left fifth interspace at the midclavicular line. In the event of electromechanical dissociation, defibrillation attempts were abandoned. The inflation/deflation and infusion cycle was then continued, pending return of VF or restoration of spontaneous circulation. If VF returned, a single 300-J countershock was delivered to the precordium. In group 2, the aorta was occluded but neither saline nor epinephrine bolus was injected; procedures were otherwise identical to that of group 1. In group 3, a bolus of epinephrine was injected in amounts of 30 μg/kg into the right atrium beginning at 30 seconds after start of precordial compression. Contingent on magnitude and duration of the pressor effect, the injections were repeated with the intent to maintain coronary perfusion pressure within the range of 25 to 30 mm Hg throughout the resuscitation interval for a maximum of 10 injections. Beginning 30 seconds after start of precordial compression, 30-mL boluses of oxygenated saline were infused into the ascending aorta at 1-minute intervals. In group 4, the procedures were identical to those of group 3 except that no oxygenated saline was injected.

Restoration of spontaneous circulation was defined as the return of a supraventricular rhythm with a mean aortic pressure of 60 mm Hg for a minimum of 5 minutes. Failure to resuscitate after 30 minutes was defined as nonresuscitability. Resuscitated animals were observed for an interval of 4 hours under critical care conditions. Except for mechanical ventilation and infrared heating lamps to maintain body temperature within the specified range, no other resuscitative interventions and specifically no vasopressor agents were used for management in the postresuscitation interval. After 4 hours, the endotracheal tube, vascular catheters, and electrodes were removed. The animals were then returned to their cages and observed for an additional interval of 48 hours. The neurological deficit score was recorded at 24-hour intervals.

Statistical Analysis

Data are presented as mean±SD unless otherwise stated. For continuous data, differences among the four groups were analyzed by ANOVA using the Scheffé method for multiple comparison. The outcome differences were analyzed with Fisher’s exact test. A P value of <.05 was regarded as significant.

Results

No spontaneous reversal of VF was observed. Each of the animals that received either combined proximal aortic balloon occlusion with infusion (group 1) or proximal balloon occlusion alone (group 2) were successfully resuscitated after electrical defibrillation, and these animals survived for more than 48 hours. Three of 5 animals that received epinephrine with proximal aortic infusion (group 3) were successfully resuscitated. However, each of these animals manifested tachycardia, hypotension in association with progressive decreases in cardiac output, and increases in right-sided filling pressures and died within 120 minutes after successful resuscitation. Only 1 of 5 animals that received epinephrine alone (group 4) was successfully resuscitated and survived for 48 hours. There was no significant difference in the neurological deficit scores between animals.

FIG 1. Graph shows representative experiment with changes in coronary perfusion pressure (CPP) after complete occlusion of the aorta and after proximal aortic infusion in pigs. PC indicates precordial compression; B, balloon occlusion; and I, infusion.
FIG 2. Graph shows the effects of four different interventions on coronary perfusion pressure (CPP) and end-tidal CO₂ (PETCO₂) during precordial compression. Values are mean±SD.

in groups 1 and 2 at 24 hours after successful resuscitation. However, the neurological deficit was significantly less after 48 hours in animals that had both proximal occlusion and infusion (group 1; see Table). The interval between start of resuscitation efforts and return of spontaneous circulation in the animals that were successfully resuscitated was not significantly different between groups (Table).

The maximal coronary perfusion pressure and the end-tidal CO₂ were both significantly increased after proximal aortic balloon occlusion (Fig 2). There was an eightfold increase in coronary perfusion pressure from approximately 7 to 60 mm Hg during balloon inflation, and this pressure level was maintained during the 30-second interval of occlusion. When balloon occlusion was combined with proximal injection of 30 mL of oxygenated saline solution, the coronary perfusion pressure was augmented from approximately 60 mm Hg to levels exceeding 90 mm Hg (Fig 3). Autopsy demonstrated no significant internal injuries. Specifically, there was no gross evidence of injury to the endocardium of the aorta at the site of the balloon occlusion.

FIG 3. Graph shows effects of aortic balloon occlusion and infusion on coronary reperfusion pressure after 7 minutes of untreated cardiac arrest in pigs. The cumulative effects of six cycles of the combined interventions are shown together with onset of electromechanical dissociation (EMD). The spontaneous conversion of EMD to a regular rhythm and the restoration of spontaneous circulation maintained arterial pressure at approximately 100 mm Hg. VF indicates ventricular fibrillation; TACHY, tachycardia; HR, heart rate; PC, precordial compression; and CPP, coronary perfusion pressure.

Discussion

Reestablishment of myocardial blood flow is now recognized the single most critical hemodynamic determinant for successful defibrillation and for restoration of spontaneous circulation. Unfortunately, conventional external CPR often fails to generate minimal threshold levels of myocardial perfusion pressure and especially so if resuscitative efforts are delayed. It is likely that after prolonged cardiac arrest, progressive myocardial ischemic injury accounts for loss of ventricular compliance and increases in resistance to coronary blood flow. Progression of ischemia has been identified as the cause of the "stone heart," which is associated with fatal cardiac arrest. Accordingly, increasingly larger coronary perfusion pressure and blood flow would be required to maintain adequate coronary perfusion under conditions when cardiac resuscitation efforts are delayed. This has been demonstrated previously under experimental conditions of prolonged untreated cardiac arrest in both dogs and pigs by Dr Safar's group and by our own group.19-22 When coronary perfusion pressure was increased to levels exceeding 60 mm Hg by extracorporeal circulation, spontaneous circulation could be restored after intervals exceeding 15 minutes of untreated cardiac arrest. However, the routine use of emergency extracorporeal circulation is constrained by the limited availability of trained professionals, by the greater technical complexity of extracorporeal systems, and by the relatively high cost. The present experimental studies demonstrate that intermittent balloon occlusion of the ascending aorta with or without proximal infusion together with conventional precordial compression has promise as an equally or more effective alternative. It is likely to be technically less demanding, less invasive, and less costly than extracorporeal circulation or open-chest cardiac massage including postthoracotomy management.

In the porcine model used by us and in human patients, there is essentially no salvage when conventional CPR is delayed for more than 7 minutes.23 In this setting, we were unable to secure meaningful survival of the pigs with conventional techniques including maximal adrenergic vasopressor therapy after 7 minutes of untreated cardiac arrest. However, after 7 minutes of untreated cardiac arrest under such controlled conditions, intermittent ascending aortic occlusion allowed successful cardiac resuscitation and survival of pigs without or with only minimal gross neurological deficits after 48 hours.

If such techniques are to be applied to human patients, the practicality of aortic catheterization under the crisis conditions of cardiac arrest must be addressed. In the absence of direct clinical trials on patients in realistic clinical settings, the issue is not likely to be securely resolved. However, experiences with related procedures provide substantial support that it is a reasonable undertaking. In the organized in-hospital setting, femoral arterial cannulation by percutaneous techniques for instituting extracorporeal circulation may be completed within less than 5 minutes during external cardiac massage.24,25 In the clinical setting in trials under the crisis conditions of cardiogenic shock and cardiac arrest, femoral or brachial artery catheterizations alone may be completed within intervals of less than 2 minutes.26,27 We also recognize that fluoroscopic
facilities are not likely to be routinely available for placement of the balloon catheter under the emergency conditions of CPR. However, preliminary trials in 11 animals demonstrate the feasibility of advancing an appropriately curved balloon catheter into appropriate position guided by external measurement of body length and without fluoroscopic guidance.

With ascending aortic occlusion and therefore intermittent arrest of cerebral blood flow, there is also the potential of cerebral ischemic injury, and the ultimate success of cardiac resuscitation is contingent on cerebral salvage. The studies by Safar et al provide evidence that normothermic cardiac arrest of up to 15 minutes could be reversed without significant neurological deficit. When, in baboons and monkeys, cerebral blood flow is reduced to only 10% of normal for intervals as long as 2 hours, essentially normal cerebral function may be restored. The results of the present studies and specifically the low neurological deficit scores after intermittent occlusion of aortic blood flow provide evidence that the technique is not likely to generate disproportionately large numbers of CPR survivors with cerebral ischemic injury. Yet the present study was designed to test the capability of the aortic balloon occlusion technique to resuscitate the arrested heart. More specific investigations that address the cerebral effect of proximal aortic occlusion and the optimal time interval for minimizing the potential of cerebral ischemic injury in settings of cardiac resuscitation are pending.

Aortic balloon counterpulsation was previously investigated for resuscitation after cardiac arrest. Coletti and coworkers used a balloon catheter that was advanced into the descending thoracic aorta in a dog. Resuscitation for VF was attempted by open-chest direct cardiac compression beginning 15 seconds after VF was induced. When the balloon was inflated and deflated at a rate of 100/min with an inflation/deflation ratio of 1:4, the coronary perfusion pressure increased from 28 to 64 mm Hg, and this was accompanied by increases in coronary blood flow from 15 to 28 mL/min. Wesley and Morgan advanced a balloon catheter into the descending thoracic aorta of dogs to occlude the infradiaphragmatic aortic flow during open-chest cardiac compression. With balloon occlusion, the coronary perfusion pressure increased from 33 to 48 mm Hg. However, their reports were not extended to indicate effects on resuscitability and survival. Emeran and coworkers further investigated balloon occlusion of the abdominal aorta with synchronized precordial compression in the dog during VF. With balloon counterpulsation, coronary perfusion pressure increased from 10 to 19 mm Hg. Accordingly, these methods of aortic counterpulsation produced moderate increases in coronary perfusion pressure and myocardial blood flow.

There is also a substantial literature on intra-arterial infusion for reversal of hypovolemia stemming from the laboratory of Negovsky and Kirimli and Safar. Safar et al also referred to proximal aortic infusion of dextran 40 for amelioration of brain damage after cardiac resuscitation to minimize postresuscitation ischemic brain damage. As yet, neither effects on resuscitability nor the efficacy of these interventions after more prolonged intervals of untreated cardiac arrest have been reported. In the present study, the rationale for use of retroaortic infusion combined with balloon occlusion was to add additional volume to the forward blood flow generated by precordial compression. Even though the coronary perfusion pressure was significantly increased by retroaortic infusion in group 1, no benefit in addition to balloon occlusion was demonstrated. However, we leave open the possibility that retroaortic infusion of sanguineous blood substitute or autologous blood combined with balloon occlusion may favor outcome after even more prolonged intervals of untreated cardiac arrest. This is the subject of ongoing research.

Conclusions

Intermittent proximal balloon occlusion during external chest compression, in the experimental setting of the studies herein reported, is much more effective than pharmacological intervention with conventional external CPR, including vasopressor doses of epinephrine. Intermittent ascending aortic occlusion may therefore be viewed as a promising alternative to extracorporeal circulation and direct (open-chest) cardiac compression for cardiac resuscitation after prolonged cardiac arrest. It has the potential advantages of speed, technical ease, and lesser invasiveness.

Acknowledgments

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References

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