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Adverse Hemodynamic Effects of Interrupting Chest Compressions for Rescue Breathing During Cardiopulmonary Resuscitation for Ventricular Fibrillation Cardiac Arrest

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Background—Despite improving arterial oxygen saturation and pH, bystander cardiopulmonary resuscitation (CPR) with chest compressions plus rescue breathing (CC+RB) has not improved survival from ventricular fibrillation (VF) compared with chest compressions alone (CC) in numerous animal models and 2 clinical investigations.

Methods and Results—After 3 minutes of untreated VF, 14 swine (32 ± 1 kg) were randomly assigned to receive CC+RB or CC for 12 minutes, followed by advanced cardiac life support. All 14 animals survived 24 hours, 13 with good neurological outcome. For the CC+RB group, the aortic relaxation pressures routinely decreased during the 2 rescue breaths. Therefore, the mean coronary perfusion pressure of the first 2 compressions in each compression cycle was lower than those of the final 2 compressions (14 ± 1 versus 21 ± 2 mm Hg, $P<0.001$). During each minute of CPR, the number of chest compressions was also lower in the CC+RB group (62 ± 1 versus 92 ± 1 compressions, $P<0.001$). Consequently, the integrated coronary perfusion pressure was lower with CC+RB during each minute of CPR ($P<0.05$ for the first 8 minutes). Moreover, at 2 to 5 minutes of CPR, the median left ventricular blood flow by fluorescent microsphere technique was 60 mL $\cdot$ 100 g^{-1} $\cdot$ min^{-1} with CC+RB versus 96 mL $\cdot$ 100 g^{-1} $\cdot$ min^{-1} with CC, $P<0.05$. Because the arterial oxygen saturation was higher with CC+RB, the left ventricular myocardial oxygen delivery did not differ.

Conclusions—Interrupting chest compressions for rescue breathing can adversely affect hemodynamics during CPR for VF. (***Circulation***. 2001;104:2465-2470.)

Key Words: cardiopulmonary resuscitation ■ heart arrest ■ hemodynamics ■ fibrillation ■ ventilation

Defibrillation is the treatment of choice for ventricular fibrillation (VF).[1] Until a defibrillator is available, maintenance of myocardial viability with cardiopulmonary resuscitation (CPR) can be lifesaving. Although this approach has resulted in survival rates of 25% to 30% in Seattle, dismal survival rates of <5% are generally reported elsewhere.[1–3] One contributing factor to the very low survival rates in 3 relatively recent studies may be the disappointingly low rates of bystander-initiated CPR: 16%, 28%, and 22%.[1–3] Although the reasons for such low bystander CPR rates are not fully known, mouth-to-mouth rescue breathing is apparently a barrier to the performance of bystander CPR.[1–4]

Numerous animal investigations and 2 clinical studies suggest that bystander CPR with chest compressions alone (CC) is as effective as chest compressions plus rescue breathing (CC+RB) for VF cardiac arrest.[5–14] This technique is attractive because it is simpler than standard CPR and easier to teach, learn, remember, and perform.[2–4,14]

Hypoxia and hypercarbia, however, are important mediators of poor outcome from VF.[10,15] Experimental investigations comparing CC with CC+RB have established that CC can maintain adequate arterial oxygen saturation for 4 to 10 minutes.[5–10,16] Nevertheless, CC results in lower arterial oxygen saturation and more severe hypercarbic acidosis than CC+RB. Therefore, CC has been presumed to be less effective at delivering oxygen to the myocardium than CC+RB.

In a recent animal investigation, qualitative retrospective review of the aortic and right atrial pressure waveforms during simulated single-rescuer CPR demonstrated substantial decreases in the aortic diastolic pressures and coronary perfusion pressures (CPPs) during the 4-second interval for the 2 rescue breaths.[11] The aortic pressure and CPP promptly increased during the first 3 to 7 chest compressions of the next series of 15 consecutive compressions. Perhaps adverse

effects of rescue breathing on CPR hemodynamics counterbalance the improved arterial oxygenation.

This investigation was undertaken to evaluate and quantify the effects of simulated rescue breathing on myocardial hemodynamics and oxygen delivery during simulated bystander CPR for VF cardiac arrest. We hypothesized that CC+RB would improve arterial oxygen saturation and worsen myocardial perfusion compared with CC alone. We further hypothesized that myocardial oxygen delivery would not differ in the 2 groups, resulting in similar successful resuscitation rates.

Methods

Animal Preparation

Experimental protocols were approved by The University of Arizona Institutional Animal Care and Use Committee and followed the guidelines of the American Physiological Society. Healthy domestic pigs (32 ± 1 kg) were subjected to masked anesthesia with isoflurane, followed by oral endotracheal intubation. They were mechanically ventilated with a volume-limited, time-cycled Harvard ventilator (model 661, Harvard Apparatus, Inc) on a mixture of room air and titrated isoflurane (generally 0.5% to 1.5% inspired concentration). The tidal volume was initially set at 15 mL/kg and the ventilator rate at 12 breaths per minute; ventilator settings were adjusted to maintain end-tidal carbon dioxide at 35 to 40 mm Hg.

After a surgical plane of anesthesia had been achieved, introducer sheaths were placed in the right internal and external jugular veins, right carotid artery, and right femoral artery by cutdown technique. High fidelity, solid-state, micromanometer-tipped catheters (MPC-500, Millar Instruments) were advanced through the carotid artery into the left ventricle and through the femoral artery and external jugular vein into thoracic locations. Catheter placements were performed under fluoroscopic guidance.

Measurements

Right atrial pressure and aortic pressure, as well as ECG and end-tidal P_{CO_2} measurements (model 47210A, Hewlett Packard), were continuously displayed and recorded on a laptop computer (Fujitsu Lifebook 530T) with specialized data acquisition software (Windaq, Dataq Instruments Inc) throughout the experiment until the 1-hour simulated intensive care unit period ended. CPP during CPR was calculated by subtracting mid-diastolic right atrial pressure from mid-diastolic aortic pressure. The integrated CPP (iCPP), or positive area under the curve, was also measured during each minute of CPR. Arterial blood gas specimens were obtained from the thoracic aorta at baseline (before cardiac arrest) and 5 and 15 minutes after cardiac arrest (2 and 12 minutes after chest compressions were started). Oxygen saturation, P_{CO_2}, P_{O_2}, pH, and hemoglobin were measured with a blood gas analyzer (IL-1306 with model 482 co-oximeter, Instrumentation Laboratories). Minute ventilation during minute 7 of CPR was determined with a heated pneumotachometer (Fleisch size 0, Instrumentation Associates) attached to a well-sealed nose cone mask.

Left ventricular myocardial blood flow and cardiac output were determined with a fluorescent, nonradioactive, color-microsphere technique at baseline (before cardiac arrest), between minutes 2 and 5 of CPR (5 to 8 minutes after VF), and between minutes 9 and 12 of CPR (12 to 15 minutes after VF).[9,10,17] Fluorescent, colored polystyrene–divinyl benzene microspheres, 12 ± 2 μm (E-Z Trac), were injected as a bolus ($\approx10\times10^6$ spheres) into the left ventricle. Reference aortic blood samples were obtained over 2 minutes 35 seconds at a rate of 10 mL/min by automatic screw pump (Harvard Apparatus, Inc). The left ventricle was sectioned and microspheres were counted as previously reported.[9,10,17]

Experimental Protocol

After baseline data were collected, a pacing electrode was positioned in the right ventricle. Isoflurane was discontinued and the aortic pressure allowed to return to baseline (systolic pressure >80 mm Hg). VF was then induced with a 60-cycle alternating current to the endocardium and confirmed by the ECG waveform and precipitous decline in aortic pressure. Ventilation was discontinued. A 3-minute interval of untreated VF, mimicking a bystander recognizing cardiac arrest and calling for help, was followed by 12 minutes of basic life support. Animals were randomly assigned to (1) the CC group, provided with a metronome-guided rate of 100 compressions per minute, punctuated each minute with a brief rest period for the rescuer to take 2 deep breaths, or (2) the CC+RB group, provided with 2 manual rescue breaths followed by 15 manual chest compressions at the metronome-guided rate of 100 compressions per minute, repeated sequentially. The rescue breaths were provided with a gas mixture of 17% oxygen and 4% carbon dioxide, simulating expired air from a rescuer.[2] Endotracheal tubes remained in place during CPR to protect the airway and avoid gastric distention with rescue breaths. The same research technician performed chest compressions in all animals. He compressed the pig's chest approximately one third of the anteroposterior diameter. All animals in both groups gasped during CPR.

At the end of this simulated bystander CPR period, 15 minutes after VF was induced, all animals received advanced cardiac life support according to American Heart Association algorithms for VF, as if the paramedic unit had arrived at the scene.[1] Electrical shock therapy was provided, starting with 120 J (≈4 J/kg) on the first 2 shocks and 200 J (≈6 J/kg), if necessary, on the third and all subsequent shocks. CPR by this simulated paramedic team included ventilation with 100% oxygen on a volume-cycled ventilator at a rate of 15 breaths per minute and chest compressions manually at a rate of 100 per minute. Restoration of spontaneous circulation was defined as unassisted pulse with a systolic arterial pressure >50 mm Hg and a pulse pressure >20 mm Hg lasting >1 minute. If the animal did not attain return of spontaneous circulation with the first set of shocks, epinephrine (0.02 mg/kg) was immediately administered intravenously. After each epinephrine administration, CPR was continued for 1 minute to allow for circulation of the epinephrine before further attempts to defibrillate.

All successfully resuscitated animals were supported aggressively for 1 hour in a simulated intensive care setting. All pigs received 40 mL/kg IV of normal saline during the intensive care period, because they had received no fluids the previous night and suffered "third space" losses from their significant cardiovascular and surgical insults. Mechanical ventilation was provided with 100% oxygen and adjusted to obtain an end-tidal carbon dioxide of 30 to 40 mm Hg. At the end of 1 hour, all animals were weaned off pharmacological and ventilatory support. Throughout the intensive care period, isoflurane was administered, as necessary, to maintain adequate analgesia and anesthesia. Animals that survived the intensive care period were transferred to observation cages for the next 24 hours.

Outcome and Neurological Evaluation

Survival and neurological status were evaluated at 24 hours after the initial cardiac arrest. To provide objective neurological evaluation, swine cerebral performance categories were assessed.[5,6,9–11] Briefly, swine cerebral performance category is a global assessment of neurological function. Category 1 was assigned to pigs that appeared normal on the basis of level of consciousness, gait, feeding behavior, response to an approaching human, and response to human restraint. Category 2, mildly abnormal, was assigned when the pigs had subtle dysfunction with regard to these characteristics. Category 3, severely disabled, referred to more severe dysfunction, such as inability to stand, walk, or eat. Category 4, vegetative state or deep coma, referred to pigs with minimal response to noxious stimuli. Category 5 referred to animals with no response to their environment. Categories 1 and 2 were considered good neurological outcome.
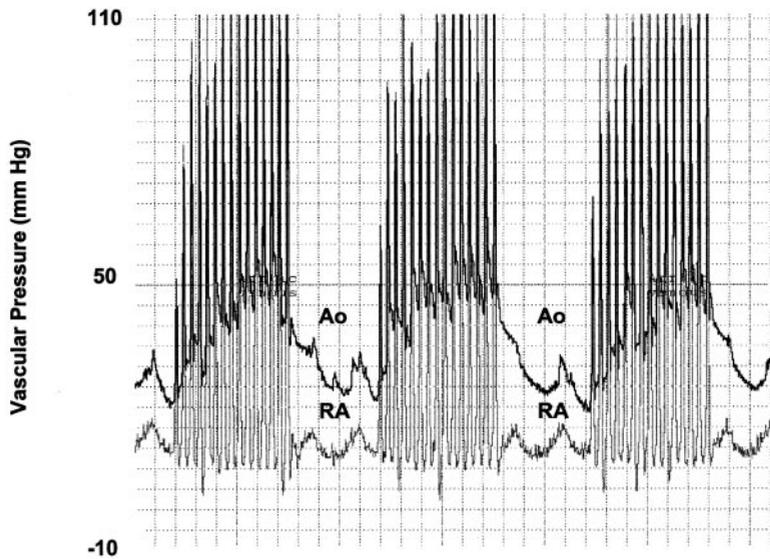
Figure 1. Aortic (Ao, dark band) and right atrial (RA, light band) pressures during standard CPR, CC+RB, with a 15:2 compression:ventilation ratio. Aortic relaxation, or diastolic, pressure (lower border of dark band) decreases during each set of 2 breaths, resulting in lower CPP during first several compressions of next cycle. Right atrial relaxation, or diastolic, pressure is most inferior border. Difference between Ao and RA relaxation pressures is CPP.

Data Analysis

Continuous variables such as blood pressures, CPP, iCPP, and blood gas analyses were evaluated by 2-tailed, unpaired Student's t test and described as mean±SEM. Continuous variables that were not normally distributed (myocardial blood flows, cardiac outputs, and oxygen deliveries) were evaluated by Mann-Whitney U test and described as median (25%, 75%). In the CC+RB group, we compared the mean CPP during the first 2 compressions of each 15-compression cycle with the last 2 compressions by paired Student's t test. Comparisons of discrete variables, such as rate of return of spontaneous circulation, 1-hour ICU survival, swine cerebral performance categories, 24-hour survival, and 24-hour good neurological outcome were evaluated by Fisher's exact test.

Results

For the CC+RB group, the aortic relaxation ("diastolic") pressures routinely decreased during the interval of 2 rescue breaths when no compressions were provided, thereby also decreasing the CPPs (Figure 1). Therefore, the mean CPP of the first 2 compressions in each compression cycle was lower than that of the final 2 compressions (14±1 versus 21±2 mm Hg, respectively, $P<0.001$). This difference was

demonstrable independently at each minute of the 12 minutes of CPR (Figure 2).

Thirteen of the 14 animals survived 24 hours with good neurological outcome. Six of the 7 CC animals and 5 of the 7 CC+RB animals were in cerebral performance category 1 at 24 hours (ie, normal); 1 in each group was in cerebral performance category 2, mildly abnormal; and 1 CC+RB animal was in cerebral performance category 3, severely disabled. All 13 animals with good neurological outcome could stand, walk, feed themselves, and actively resist restraint. Animals in cerebral performance category 1 performed these tasks normally; animals in cerebral performance category 2 had slightly wobbly gaits, lethargy, or sluggish response to restraint. The only animal in category 3 could not walk and responded quite sluggishly to restraint but would drink.

At baseline, the CC and CC+RB groups did not differ in weight, hemoglobin concentration, heart rate, blood pressure, or central venous pressure. Aortic and right atrial compression pressures during each minute of CPR did not differ between the 2 groups (Table 1). At each minute of CPR, the
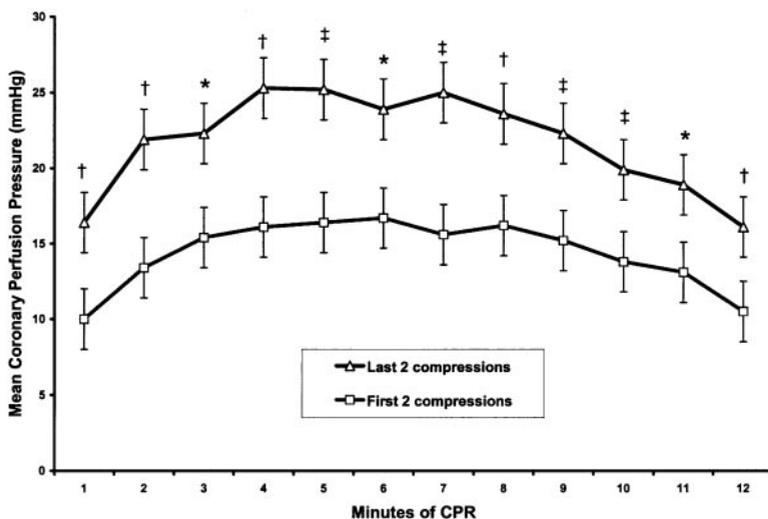
Figure 2. Mean CPP of first 2 compressions (bottom line) and last 2 compressions (top line) of each 15-compression cycle during CPR with CC+RB at a compression:ventilation ratio of 15:2. Mean CPP difference: *$P<0.05$; †$P<0.01$; ‡$P<0.001$.
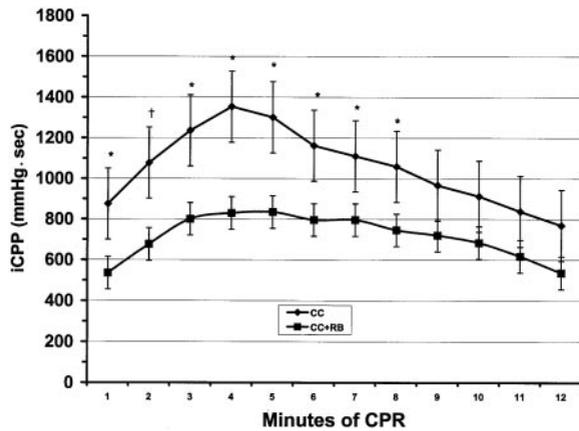
Figure 3. iCPP over each minute in CC and CC+RB groups. iCPP difference: *$P<0.05$; †$P<0.01$.

CPP at the end of the 15-compression cycle with CC+RB did not differ from the CPP with CC (Table 1). None of the animals received inotropic or vasopressor support after return of spontaneous circulation.

During each minute of CPR, the number of chest compressions delivered was lower in the CC+RB group (62 ± 1 versus 92 ± 1 mm Hg, $P<0.001$). Because of metronome guidance, these compression rates were remarkably consistent during each minute of CPR. The iCPP was lower with CC+RB during each minute of CPR, $P<0.05$ for each of the first 8 minutes of CPR (Figure 3).

There were no differences in cardiac output, left ventricular myocardial blood flow, or left ventricular myocardial oxygen delivery between the 2 groups at baseline (Table 1). Median left ventricular blood flow early in CPR, during the interval between minutes 2 and 5 of CPR, however, was 96 (62, 130) mL · 100 g^{-1} · min^{-1} with CC versus 60 (20, 100) mL · 100 g^{-1} · min^{-1} with CC+RB, $P<0.05$. After more prolonged CPR, during the interval between minutes 9 and 12 of CPR, left ventricular myocardial blood flow was 79 (27, 131) mL · 100 g^{-1} · min^{-1} with CC versus 52 (27, 77) mL · 100 g^{-1} · min^{-1} with CC+RB, $P=0.11$. The concomitant left ventricular myocardial oxygen deliveries and cardiac outputs at these times did not differ (Table 1, Figure 4).

There were no differences in arterial blood gases between the 2 groups at baseline. The arterial oxygen saturation and pH were higher and P$_{CO_2}$ lower in the CC+RB group 5 and 15 minutes after VF (ie, after 2 and 12 minutes of CPR), respectively (Table 2). Minute ventilation in the CC group after 7 minutes of CPR was 2650 ± 670 mL/min, and gasping accounted for $41\pm9\%$ of the minute ventilation.

Discussion

This investigation establishes that interrupting chest compressions for rescue breathing can adversely affect myocardial hemodynamics during CPR for VF. Compared with CC, CC+RB resulted in worse myocardial perfusion, yet better oxygen content of the blood that perfused the myocardium. The net result was no substantial difference in myocardial oxygen delivery. Not surprisingly, once again this study confirmed that successful resuscitation and neurological out-
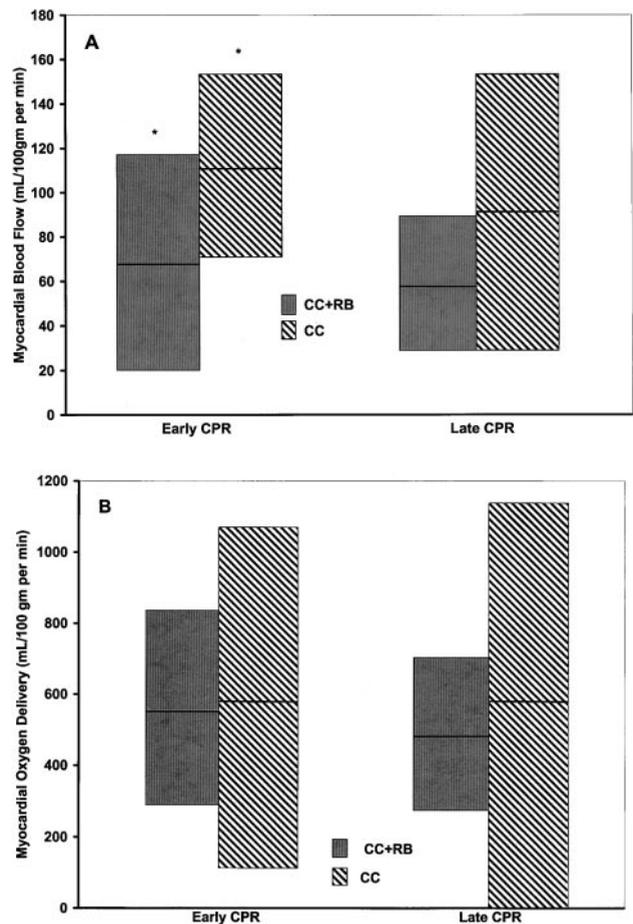
Figure 4. A, Median left ventricular myocardial blood flow in CC vs CC+RB groups with 25% and 75%. Early CPR refers to interval from 2 to 5 minutes of CPR (5 to 8 minutes after VF); late CPR refers to interval from 9 to 12 minutes of CPR (12 to 15 minutes after VF). Blood flow difference: *$P<0.05$. B, Median left ventricular myocardial oxygen delivery in 2 groups, as in A.

come are comparable after CC or CC+RB for VF cardiac arrest.[5–14] More importantly, this investigation highlights the hemodynamic importance of continuous chest compressions during CPR.

The relative time for rescue breathing and compression during single-rescuer CPR is a "zero-sum" game.[2] Indeed, the number of compressions was nearly 50% greater with CC than with CC+RB in this experiment. Moreover, we previously published qualitative data of aortic and right atrial pressure tracings during CC+RB, suggesting substantial decreases in the aortic diastolic pressures and CPPs during the 2 rescue breaths (ie, during the 4-second interval between compressions).[11] The aortic pressure and CPP promptly increased during the first 3 to 7 chest compressions of the next series of 15 consecutive compressions. The present investigation confirms this finding with quantitative data indicating that the mean CPP decreased by 7 mm Hg during the 2 rescue breaths. Most importantly, the median left ventricular myocardial blood flow was markedly lower during early CPR with CC+RB than with CC.

The mechanism responsible for the decreases in aortic diastolic pressure during the 2 rescue breaths was not delin-

TABLE 1.   Hemodynamics at Baseline and During CPR

	AoS, mm Hg	AoD, mm Hg	RAS, mm Hg	RAD, mm Hg	CPP	CO, L/min	MBF, mL · 100 g^{-1} · min^{-1}	MDO$_2$, mL · 100 g^{-1} · min^{-1}
Baseline								
CC+RB	92±4	67±5		7±1		3.3 (1.9, 4.7)	76 (3, 149)	720 (130, 1310)
CC	91±2	63±3		8±1		3.8 (2.0, 5.6)	70 (35, 105)	740 (490, 990)
Early CPR								
CC+RB	88±8	38±4	116±11	13±1	26±3	0.60 (0.3, 0.9)	60 (20, 100)*	560 (290, 830)
CC	92±9	41±6	108±22	13±1	29±6	0.90 (0.4, 1.4)	96 (62, 130)*	590 (110, 1070)
Late CPR								
CC+RB	83±6	35±4	107±6	14±2	21±4	0.50 (0.2, 0.8)	52 (27, 77)	490 (280, 700)
CC	86±5	31±5	110±10	12±1	18±4	0.70 (0.3, 1.1)	79 (27, 131)	590 (0, 1140)

AoS indicates aortic systolic pressure; AoD, aortic diastolic pressure; RAS, right atrial systolic pressure; RAD, right atrial diastolic pressure; CO, cardiac output; MBF, left ventricular myocardial blood flow; MDO$_2$, left ventricular myocardial oxygen delivery; Baseline, before VF; Early CPR, pressures at 4 minutes of CPR and flows (CO, MBF, MDO$_2$) during 2–5 minutes of CPR; and Late CPR, pressures at 11 minutes of CPR and flows during 9–12 minutes of CPR. All pressures are mean±SEM; all flows are median (25%, 75%).

*$P<0.05$ between groups.

eated. Presumably, the longer pause between compressions resulted in greater "runoff" of blood from the aorta, thereby decreasing the aortic volume and pressure.

Because of lower compression rates and lower CPP during the initial part of the compression cycle with CC+RB, the "true" mean CPP during each of the first 8 minutes of CPR was higher in the CC group, as confirmed by the iCPP data. Notably, these iCPP differences were demonstrable even though the CPP at the end of the 15-compression cycle with CC+RB did not differ from the corresponding CPP with CC (Table 1). In previous animal investigations, we consistently evaluated the CPP in 3 consecutive representative compression-relaxation cycles during each minute of CPR. The rapidly changing CPP during the first several compressions in the CC+RB group was not regarded as representative. Therefore, the calculated mean CPP in the CC and CC+RB groups did not differ in any of those studies.

Consistent with previous investigations, this study confirms that CC+RB with CPPs of 20 to 30 mm Hg can result

in left ventricular myocardial blood flow >50% of prearrest baseline despite cardiac outputs 15% to 25% of prearrest baseline.[9,18,19] Peripheral vasoconstriction and coronary vasodilation preferentially direct blood flow through the coronary arteries. Impressively, this study establishes that left ventricular myocardial blood flow during CC can be nearly the same as prearrest baseline in the setting of excellent compressions, nearly maximally dilated coronary arteries, and no coronary artery disease (Table 1).

Some aspects of this study protocol tend to bias the data in favor of the CC+RB group compared with real prehospital single-rescuer CPR. It is unlikely that excellent chest compressions and mouth-to-mouth rescue breathing would be provided by a single rescuer in the field. Transitions from rescue breathing to compressions and vice versa are likely to be much more difficult for a single rescuer than for our experienced, multi-individual research team. In fact, video data of CPR performance on resuscitation manikins immediately after a CPR course demonstrated substantially fewer chest compressions with single-rescuer CC+RB than in our experiment because of time spent on rescue breathing and the attendant transitions.[4] Those single-rescuer subjects compressed the chest only 39 times per minute, mostly because the average pause from compressions to position the head and provide 2 rescue breaths was 16 seconds. In contrast, the interval for 2 rescue breaths was only 4 seconds in our swine study, consistent with American Heart Association recommendations.[1]

Other important limitations include lack of blinding and applicability to human cardiac arrest victims. By its very nature, this study could not be blinded. Strict adherence to standardized resuscitation and postresuscitation protocols, however, was intended to minimize treatment bias. In addition, the comparability of aortic and right atrial compression pressures in the 2 groups suggests that the force of chest compressions was similar for both groups.

Compared with human CPR studies, animal CPR experiments allow for stricter experimental control and more consistent measurement of relevant physiological variables,

TABLE 2.   Arterial Blood Gases During CPR

Arterial Blood Gas	CC+RB	CC	P
Baseline, before VF			
So$_2$, %	93±1	95±2	0.49
pH	7.48±0.01	7.48±0.01	0.77
Pco$_2$, mm Hg	38±1	40±1	0.34
HCO$_3^-$, mmol/L	29±1	30±1	0.27
After 2 min of CPR			
So$_2$, %	93±1	67±9	0.01
pH	7.57±0.02	7.40±0.02	0.0002
Pco$_2$, mm Hg	25±1	42±6	0.02
HCO$_3^-$, mmol/L	23±1	26±2	0.17
After 12 min of CPR			
So$_2$, %	93±2	70±11	0.05
pH	7.48±0.03	7.33±0.06	0.04
Pco$_2$, mm Hg	22±2	43±10	0.05
HCO$_3^-$, mmol/L	16±1	20±2	0.06

thereby more effectively elucidating the mechanisms of different interventions. Nevertheless, human outcome data are the "gold standard" for resuscitation interventions. A prospective study of 3053 prehospital cardiac arrests suggests that our findings are applicable to humans.[12,13] Long-term survival was comparable among those treated with good-quality chest compressions alone (17 of 116, or 15%) and those treated with good-quality chest compressions plus mouth-to-mouth rescue breathing (71 of 443, or 16%). The outcomes with either of these techniques were superior to those receiving no CPR (123 of 2055, or 6%, $P<0.001$).

A recent study from Seattle also suggests that bystander-initiated CPR is as effective with CC as CC+RB.[14] In a randomized manner, emergency medical system telephone dispatchers gave bystanders CPR instructions for CC or CC+RB. Successful initial resuscitation resulting in hospital admission was not different (97 of 241 [40%] with CC versus 95 of 279 [34%] with CC+RB, $P=0.15$). Similarly, survival to hospital discharge was not different (35 of 240 [15%] with CC versus 29 of 278 [10%] with CC+RB, $P=0.18$).

In summary, this investigation establishes that interrupting chest compressions for rescue breathing can adversely affect hemodynamics during CPR. We postulate that avoiding these interruptions is a mediator of the excellent outcomes with CC CPR in experimental models and clinical investigations of CPR for VF.

Acknowledgment

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