Vasopressor Response in a Porcine Model of Hypothermic Cardiac Arrest Is Improved with Active Compression-Decompression Cardiopulmonary Resuscitation Using the Inspiratory Impedance Threshold Valve

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During normothermic cardiac arrest, a combination of active compression-decompression (ACD) cardiopulmonary resuscitation (CPR) with the inspiratory threshold valve (ITV) significantly improves vital organ blood flow, but this technique has not been studied during hypothermic cardiac arrest. Accordingly, we evaluated the hemodynamic effects of ACD + ITV CPR before, and after, the administration of vasopressin in a porcine model of hypothermic cardiac arrest. Pigs were surface-cooled until their body core temperature was 26°C. After 10 min of untreated ventricular fibrillation, 14 animals were randomly assigned to either ACD CPR with the ITV ($n = 7$) or to standard (STD) CPR ($n = 7$). After 8 min of CPR, all animals received 0.4 U/kg vasopressin IV, and CPR was maintained for an additional 10 min in each group; defibrillation was attempted after 28 min of cardiac arrest, including 18 min of CPR. Before the administration of vasopressin, mean ± SEM common carotid blood flow was significantly higher in the ACD + ITV group compared with STD CPR (67 ± 13 versus 26 ± 5 mL/min, respectively; $P < 0.025$). After vasopressin was given at minute 8 during CPR, mean ± SEM coronary perfusion pressure was significantly higher in the ACD + ITV group, but did not increase in the STD group (29 ± 3 versus 15 ± 2 mm Hg, and 25 ± 1 versus 14 ± 1 mm Hg at minute 12 and 18, respectively; $P < 0.001$); mean ± SEM common carotid blood flow remained higher at respective time points (33 ± 8 versus 10 ± 3 mL/min, and 31 ± 7 versus 7 ± 3 mL/min, respectively; $P < 0.01$). Without active rewarming, spontaneous circulation was restored and maintained for 1 h in three of seven animals in the ACD + ITV group versus none of seven animals in the STD CPR group (not significant). During hypothermic cardiac arrest, ACD CPR with the ITV improved common carotid blood flow compared with STD CPR alone. Moreover, after the administration of vasopressin, coronary perfusion pressure was significantly higher during ACD + ITV CPR, but not during STD CPR.

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Although mild hypothermia (34° to 36°C) may exert a protective effect on the brain during and after cardiac arrest (1,2), cardiopulmonary resuscitation (CPR) of patients with severe hypothermia (<30°C) may be extremely difficult. For example, the hypothermic heart may be unresponsive to defibrillation (3), and prolonged CPR until rewarming may result in chest injury. The current strategy during hypothermic cardiac arrest is rewarming during CPR before drug administration and defibrillation because of concerns about toxic cumulative effects of vasopressors when being used <30°C (4). An alternative strategy may be to

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KGL is the inventor of the inspiratory impedance threshold valve, and receives royalties from its sale, and therefore may have a conflict of interest; all other authors do not have a conflict of interest in regard to drugs or devices being discussed in this report.

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improve vital organ blood flow during CPR with a mechanical device and a vasopressor with subsequent defibrillation. This approach may enable rewarming with a beating heart instead of prolonged CPR for hours, which may be both faster and cause fewer adverse effects.

Active compression-decompression (ACD) CPR has been shown to generate a negative intrathoracic pressure gradient, thus enhancing venous return, and subsequently vital organ blood flow during prolonged CPR (5–8). Because hypothermia results in an increased rigidity of the thorax (9,10), and higher viscosity of the blood (11), we speculate that active chest decompression may be an appropriate technique to enhance the "bellows-like" action of the chest, thus improving CPR efficiency in hypothermic cardiac arrest. If inflow of respiratory gases is further limited with an inspiratory impedance threshold valve (ITV), equilibration of the negative intrathoracic pressure and venous return generated by active chest wall expansion may occur to a greater extend. In normothermic porcine cardiac arrest models, coronary perfusion and vital organ blood flow were significantly higher when ITV was used compared with ACD CPR alone (6,12). The ITV (ResQ-Valve™; CPR_x, Minneapolis, MN) used in this experiment is a small, single-use one-way valve that is placed between the endotracheal tube and the ventilator, thus becoming part of the ventilatory circuit. Although providing no resistance to active ventilation or expiration, the ITV functions to occlude inspiratory gas exchange during the decompression phase of CPR until an opening pressure of -20 cm H_2O is reached.

Concern has been raised about giving epinephrine during normothermic advanced cardiac life support because of its β-adrenergic adverse effects (13), which may be even more pronounced during hypothermic advanced cardiac life support, when the myocardium is more prone to electrophysiological adverse effects. We have shown that vasopressin can improve coronary perfusion pressure during hypothermic CPR (14), indicating that vasopressin may be an option in this setting. Accordingly, this hypothermic cardiac arrest study was designed to compare the effects of ACD+ ITV CPR with standard (STD) CPR, before and after the administration of vasopressin, on perfusion pressure and common carotid blood flow. This approach uses combined mechanical and pharmacological means to enhance vital organ perfusion. Our hypothesis was that there would be no differences between the two CPR techniques in regard to study end-points.

Materials and Methods

Surgical Preparations and Measurements

This project was approved by the Austrian Federal Animal Investigational Committee. Animal care and use was performed by qualified individuals, supervised by veterinarians, and all facilities and transportation complied with current legal requirements and guidelines. Anesthesia was used in all surgical interventions to prevent suffering or pain.

This study was performed according to Utstein-style guidelines (15) on 14 healthy, 12–16 wk-old, mature Tyrolean domestic pigs of both sexes, weighing 30–35 kg. The animals were fasted overnight, but had free access to water. The pigs were premedicated with azaperone (neuroleptic drug; 4 mg/kg IM) and atropine (0.1 mg/kg IM) 1 h before surgery, and anesthesia was induced with propofol (1–2 mg/kg IV). After intubation during spontaneous respiration, the pigs were ventilated with a volume-controlled ventilator (Draeger EV-A, Lübeck, Germany) with 35% O_2 at 20 breaths/min, and with a tidal volume adjusted to maintain normocapnia. Anesthesia was maintained with propofol ($6–8\ mg \cdot kg^{-1} \cdot h^{-1}$), and a single dose of piritramid (30 mg). We achieved muscle paralysis with 0.2 mg/kg pancuronium after intubation, and subsequently with repeated doses of 0.1 mg/kg pancuronium as required. Lactated Ringer's solution ($6\ mL \cdot kg^{-1} \cdot h^{-1}$), and a 3% gelatin solution ($4\ mL \cdot kg^{-1} \cdot h^{-1}$) were administered in the preparation and during the cooling phase before the induction of cardiac arrest to replace fluid and blood loss derived from artificial ventilation, and withdrawal of blood samples, respectively. A STD lead II electrocardiogram was used to monitor cardiac rhythm. Depth of anesthesia was judged according to blood pressure, heart rate, and electroencephalographic monitoring (Neurotrac; Engström, Munich, Germany). If clinical assessment or physiological measurements, such as heart rate, blood pressure, or eye twinkling indicated a decreasing level of anesthesia, additional propofol and piritramid was given. Depth of anesthesia was judged and adjusted by experienced anesthesiologists. Body temperature was maintained with a heating blanket between 38.0° (100.4°F) and 39.0°C (102.2°F) during the surgical preparation.

A 7F catheter was advanced into the descending aorta via femoral cutdown for withdrawal of arterial blood samples, and measurement of arterial blood pressure. A 5F pulmonary artery catheter was placed in the pulmonary artery via cutdown in the neck to sample mixed venous blood. Another 7F catheter was placed into the right atrium via femoral cutdown for measurement of right atrial pressure and drug administration. Aortic, right atrial, and pulmonary artery pressure were measured with saline-filled catheters attached to pressure transducers (model 1290A; Hewlett Packard, Böblingen, Germany), that were calibrated to atmospheric pressure at the level of the right atrium; pressure tracings were recorded with a data acquisition system (Dewetron Port 2000, Graz,

Austria). Coronary perfusion pressure was defined as the difference between aortic and right atrial diastolic pressure. Blood gases were measured with a blood gas analyzer (AVL 995/912; AVL Medical Instruments, Vienna, Austria), and end-tidal carbon dioxide was measured with an infrared absorption analyzer (Sirecust 960; Siemens, Erlangen, Germany).

After instrumentation for hemodynamic variables, a cervical incision was performed, and the right common carotid artery was freed from supporting tissues and subsequently instrumented with ultrasound flowprobes (Transonic, Ithaca, NY) to measure organ blood flow, as previously described (16). Before trepanation, 5 mL of local anesthetic was infiltrated into the skin overlying the skull between the eyes to provide additional anesthesia. For sampling of cerebral venous blood, a burr hole was drilled into the skull over the midline, and a catheter was placed into the sagittal sinus. All catheters were flushed with normal saline containing 5 IU/mL heparin at a rate of 3 mL/h to prevent obstruction during the preparation phase.

Experimental Protocol

The experimental protocol is outlined in Table 1. After the preparation phase, the animals were placed on a bed of crushed ice, and the entire body was further covered with ice. The ice was removed when the body core temperature reached 26°C, thus representing severe hypothermia. Fifteen minutes before cardiac arrest, 5000 U of heparin was administered IV to prevent intracardiac clot formation, a single dose of 15 mg of piritramid and 8 mg of pancuronium were given, and hemodynamic variables and blood gases were measured. A 60-V alternating current was then applied via two subcutaneous needle electrodes to induce ventricular fibrillation. Cardiopulmonary arrest was defined as the point at which the aortic pressure decreased to hydrostatic pressure, and the electrocardiogram showed ventricular fibrillation; ventilation was stopped at that point.

After 10 min of untreated cardiac arrest, 14 animals were randomly assigned to either ACD CPR combined with the ITV ($n = 7$) or STD CPR ($n = 7$). CPR was performed at 100 compressions/min with a pneumatically driven automatic piston device for CPR (ACD Controller; Ambu, Glostrup, Denmark). Compression excursion was measured visually with a ruler attached to the piston housing, and continuously recorded with the data acquisition system; depth of compression was 25% of the transthoracic diameter. All animals were bag-valve ventilated with pure oxygen every fifth compression. All investigators were blinded to hemodynamic and end-tidal carbon dioxide monitor tracings.

After 8 min of CPR, all animals received vasopressin 0.4 U/kg IV. All drugs were diluted to 10 mL of normal saline and subsequently injected into the right atrium, followed by a 20-mL saline flush (investigators were blinded to the drugs). Hemodynamic variables were measured before the induction of cardiac arrest, after 4 and 8 min of CPR, and at 2, 4, 6, and 8 min after drug administration. After 28 min of cardiac arrest, including 18 min of CPR, up to 5 countershocks were administered with an energy of 100, 150, and 200 J. If ventricular fibrillation, asystole, or pulseless electrical activity was present after defibrillation, CPR was resumed, and an additional dose of vasopressin (0.4 U/kg) was given; defibrillation was performed again at 8 min after drug administration if ventricular fibrillation was observed. During this phase, external rewarming was initiated by the use of a heating blanket (Bair Hugger; Augustine Medical, Eden Prairie, MN). Return of spontaneous circulation was defined as an unassisted pulse with a systolic blood pressure of at least 50 mm Hg lasting at least 5 min. In the postresuscitation period, hemodynamic variables were measured at 5, 15, 30, and 60 min after return of spontaneous circulation. After completion of the experimental protocol, the animals were killed with an overdose of pentobarbital and potassium chloride. All pigs were autopsied to verify correct positioning of the catheters and examined for rib cage injury.

All variables were given as mean ± SEM. One-way analysis was used to determine statistical significance between the two groups. Fisher's exact test was used for analysis of return of spontaneous circulation rates. Statistical significance was considered at $P < 0.05$.

Results

Before surface cooling, at 26°C body core temperature, and before drug administration during CPR, there were no statistically significant differences in temperature, weight, and hemodynamics between groups (Table 2). In both groups, the amount of propofol and piritramid needed for sufficient analgesia was comparable. Although heart rate decreased significantly during the induction of hypothermia, none of the animals developed cardiac arrhythmias such as ectopic beats or spontaneous ventricular fibrillation. At 26°C, mean ± SEM coronary perfusion pressure (67 ± 7 versus 65 ± 4 for ACD + ITV versus STD CPR) and common carotid blood flow (270 ± 50 versus 238 ± 32 for ACD + ITV versus STD CPR) did not significantly differ between the groups. Mean ± SEM coronary perfusion pressure at minute 4 and 8 during ACD + ITV versus STD CPR was comparable (Fig. 1). Common carotid blood flow was significantly higher in the ACD + ITV group than during STD CPR at respective time points. After vasopressin, coronary perfusion pressure was significantly higher in the ACD + ITV group, but not

Table 1. Flow Chart of the Experimental Protocol

Preparation, cooling, min			VF, min		Cardiopulmonary resuscitation, min						Postresuscitation phase, min			
0	180	26°C	0	10	0	4	8	10	12	16	18	5	15	30	60
	●▼					●▼	●	●▼	●▼	●▼	●▼	●▼	●▼	●▼	●▼
							↑ Vasopressin								
											Defibrillation ↑				

VF = ventricular fibrillation, ● = sampling of blood gases, ▼ = measurement of hemodynamic variables. Note that the timeline is not subject to scale.

Table 2. Hemodynamic Variables at Prearrest and During Cardiopulmonary Resuscitation

			Cardiopulmonary resuscitation			
			Before vasopressin		After vasopressin	
	Prearrest I	Prearrest II	4 min	8 min	12 min	18 min
HR, bpm						
ACD + ITV	89 ± 5	66 ± 5	—	—	—	—
STD	94 ± 6	57 ± 2	—	—	—	—
MAP, mm Hg						
ACD + ITV	82 ± 4	59 ± 6	29 ± 2	32 ± 2	46 ± 3*	45 ± 2*
STD	87 ± 2	55 ± 4	23 ± 4	22 ± 3	29 ± 3	29 ± 3
MPAP, mm Hg						
ACD + ITV	16 ± 1	16 ± 2	—	—	—	—
STD	18 ± 1	15 ± 1	—	—	—	—
MRAP, mm Hg						
ACD + ITV	5 ± 1	6 ± 2	—	—	—	—
STD	6 ± 1	5 ± 1	—	—	—	—
Ao systolic, mm Hg						
ACD + ITV	110 ± 3	75 ± 8	50 ± 5	54 ± 5*	66 ± 4*	69 ± 4*
STD	116 ± 3	71 ± 4	39 ± 8	37 ± 6	43 ± 6	41 ± 5
Ao diastolic, mm Hg						
ACD + ITV	68 ± 5	51 ± 5	19 ± 1	20 ± 1*	37 ± 3*	32 ± 1*
STD	72 ± 2	47 ± 4	15 ± 2	15 ± 2	23 ± 2	22 ± 2
$P_{ET}CO_2$, mm Hg						
ACD + ITV	41 ± 0	12 ± 1	9 ± 1	9 ± 1*	5 ± 1*	4 ± 1*
STD	42 ± 1	12 ± 1	6 ± 1	5 ± 1	3 ± 0	2 ± 0
Temperature, °C						
ACD + ITV	38.2 ± 0.2	25.0 ± 0.2	25.2 ± 0.1	25.2 ± 0.1	25.2 ± 0.1	25.2 ± 0.1
STD	38.8 ± 0.3	25.2 ± 0	25.2 ± 0.1	25.2 ± 0.1	25.2 ± 0.1	25.2 ± 0.1

Values are mean ± SEM.
Seven animals in each group were included during the entire study period of 18 min.
Prearrest I = measurements before induction of cardiac arrest at normothermia, prearrest II = measurements before induction of cardiac arrest after hypothermia was achieved, HR = heart rate, MAP = mean arterial pressure, MPAP = mean pulmonary artery pressure, MRAP = mean right atrial pressure, Ao = aortic pressure, $P_{ET}CO_2$ = end-tidal carbon dioxide pressure, ACD + ITV = active compression-decompression and impedance threshold valve, STD = standard compression.
* $P < 0.05$ ACD versus STD.

during STD CPR (Fig. 1). Common carotid blood flow remained higher at respective time points (Fig. 2). There were no statistically significant differences in arterial blood Po_2 and Pco_2 gradient values after 4 min of CPR (Table 3). At 8 and 18 min of CPR, the Pao_2 levels were significantly lower in the ACD + ITV group compared with STD CPR, but Pao_2 levels were >150 torr. In contrast, the arterial/mixed venous Pco_2 gradient values were higher in the STD CPR group after 8 min of CPR. Moreover, the arterial/sagittal sinus Pco_2 gradient was also significantly higher in the STD CPR group at 10 min after drug administration, thus being indicative of reduced cerebral blood flow. After 28 min of cardiac arrest, including 10 min of untreated cardiac arrest and 18 min of CPR, all animals were defibrillated up to 5 times. Spontaneous circulation was restored and maintained for 1 h in 3 of 7 animals in the ACD + ITV group versus 0 of 7 animals in the STD CPR group ($P = 0.06$). In those animals without successful defibrillation (4 ACD + ITV and 7 STD animals), the second vasopressin dose did not improve perfusion pressures above the level

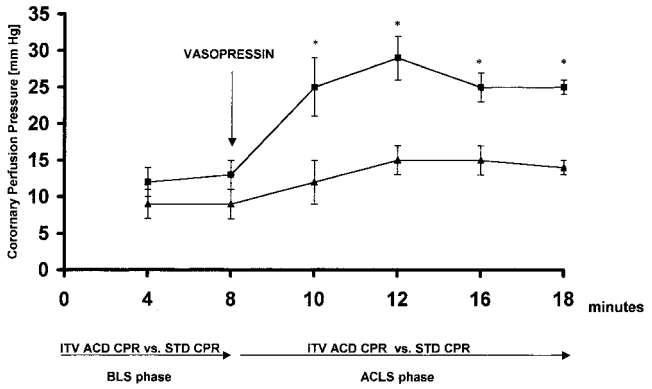

Figure 1. Mean ± SEM coronary perfusion pressure before and after drug administration. Vasopressin indicates the administration of 0.4 U/kg vasopressin IV, CPP = coronary perfusion pressure, ■ = active compression-decompression (ACD) and inspiratory threshold valve (ITV), ▲ = standard (STD) compression. BLS CPR = basic life support cardiopulmonary resuscitation, ACLS = advanced cardiac life support; *$P < 0.05$.

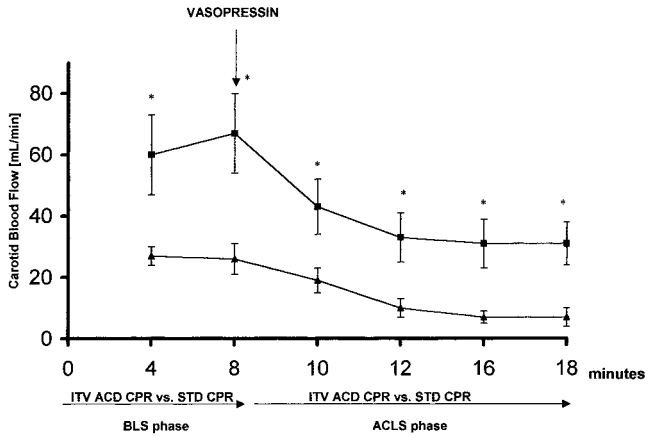

Figure 2. Mean ± SEM common carotid blood flow before and after drug administration. Vasopressin indicates the administration of 0.4 U/kg vasopressin IV, ■ = active compression-decompression (ACD) and inspiratory threshold valve (ITV), ▲ = standard (STD) compression. BLS CPR = basic life support cardiopulmonary resuscitation, ACLS = advanced cardiac life support; *$P < 0.05$.

before the first defibrillation series, and the attempt of external rewarming with hot air did not increase core temperature. Accordingly, the second defibrillation series after 8 additional minutes of CPR did not restore spontaneous circulation in the remaining animals.

Discussion

In this animal model of hypothermic cardiac arrest, ACD CPR + ITV resulted in significantly higher common carotid artery blood flow values compared with STD CPR. However, coronary perfusion pressure did not significantly differ between groups before drug administration. When vasopressin was administered after 18 minutes of cardiac arrest including 8 minutes of CPR, coronary perfusion pressure increased significantly in animals treated with ACD CPR + ITV. Common carotid artery blood flow remained higher with ACD CPR + ITV compared with STD CPR, but decreased after vasopressin.

The current STD of care for hypothermic cardiac arrest is the same as for normothermic cardiac arrest. If core temperature is <30°C (86°F), successful conversion to normal sinus rhythm may not be possible until rewarming is accomplished (17). Because most rapid core rewarming strategies (i.e., peritoneal lavage or extracorporal circulation) are not available in the prehospital phase, CPR must often be performed even during prolonged transport times. Accordingly, the outcome of patients with hypothermic cardiac arrest is quite poor, and may be determined by the ability to sufficiently maintain vital organ blood flow with external chest compressions until definitive care.

One approach to improve efficiency of chest compressions may be ACD CPR. It is based on the concept that decreasing intrathoracic pressure during the decompression phase of chest compression enhances venous blood return to the thorax, thus "priming the pump" for the subsequent chest compression (5–8). Use of the ITV creates an even greater vacuum during decompression, and blood return to the thorax is further enhanced (18). The combination of both devices improves coronary perfusion pressure, and vital organ blood flow in both animal studies and a first small clinical trial (7,12,19). Thus, the American Heart Association and the European Resuscitation Council have recommended ACD CPR and the ITV as an acceptable, useful, and safe device for performance of CPR (Class IIb) (20).

Under conditions of constant minute ventilation, end-tidal carbon dioxide values increased to higher peak values in the ACD ITV group compared with STD CPR, whereas Pao_2 values decreased. The latter issue may be caused by pulmonary atelectasis, and subsequent intrapulmonary right-to-left shunt during active decompression of the chest, and intermittent airway occlusion. However, these values remained within normal physiological limits throughout 18 minutes of CPR when supplemental oxygen was used (21). Furthermore, the arteriovenous carbon dioxide gradient remained at lower levels in the ACD ITV group compared with STD CPR. Idris et al. (22) showed that increased end-tidal carbon dioxide and decreased arteriovenous carbon dioxide gradient values are associated with an increased pulmonary blood flow. Our current results and previous investigations suggest that ACD CPR combined with the ITV may also improve overall circulation during hypothermic cardiac arrest. We found common carotid artery blood flow to be significantly higher in the ACD + ITV

Table 3. Blood Gas Variables at Prearrest and During Cardiopulmonary Resuscitation

			Cardiopulmonary resuscitation			
			Before vasopressin		After vasopressin	
	Prearrest I	Prearrest II	4 min	8 min	12 min	18 min
Po_2 torr (arterial)						
ACD + ITV	122 ± 4*	196 ± 13	182 ± 40	169 ± 31*	161 ± 19*	167 ± 42*
STD	100 ± 7	190 ± 16	256 ± 49	297 ± 41	280 ± 45	330 ± 16
Po_2 torr (mixed venous)						
ACD + ITV	41 ± 2	47 ± 3	27 ± 2	31 ± 2	37 ± 5	30 ± 2
STD	37 ± 1	57 ± 10	24 ± 1	26 ± 1	30 ± 3	29 ± 2
Po_2 torr (sagittal sinus)						
ACD + ITV	43 ± 10	37 ± 2	30 ± 2	35 ± 2	49 ± 3*	41 ± 2*
STD	53 ± 14	44 ± 13	26 ± 1	29 ± 1	38 ± 4	32 ± 3
ΔPco_2 torr (arterial/mixed venous)						
ACD + ITV	5 ± 1	5 ± 1*	18 ± 4	15 ± 4*	15 ± 5	14 ± 6
STD	5 ± 1	2 ± 1	25 ± 3	27 ± 3	26 ± 5	30 ± 5
ΔPco_2 torr (arterial/sagittal sinus)						
ACD + ITV	10 ± 1	11 ± 2	39 ± 5	32 ± 2	31 ± 9	12 ± 5*
STD	10 ± 1	9 ± 1	38 ± 6	39 ± 6	41 ± 5	31 ± 7
pH units (arterial)						
ACD + ITV	7.5 ± 0.01	7.61 ± 0.01	7.54 ± 0.03	7.50 ± 0.03*	7.52 ± 0.03	7.60 ± 0.04*
STD	7.48 ± 0.01	7.62 ± 0.01	7.64 ± 0.05	7.64 ± 0.05	7.62 ± 0.04	7.75 ± 0.04
pH units (mixed venous)						
ACD + ITV	7.45 ± 0.01	7.56 ± 0.01	7.38 ± 0.01	7.38 ± 0.01	7.39 ± 0.02	7.44 ± 0.03
STD	7.45 ± 0.01	7.58 ± 0.01	7.4 ± 0.01	7.36 ± 0.01	7.36 ± 0.01	7.38 ± 0.03
pH units (sagittal sinus)						
ACD + ITV	7.41 ± 0.01	7.51 ± 0.01	7.29 ± 0.03	7.29 ± 0.02	7.30 ± 0.05	7.47 ± 0.04
STD	7.41 ± 0.01	7.52 ± 0.01	7.34 ± 0.04	7.31 ± 0.04	7.27 ± 0.03	7.37 ± 0.04

Values are mean ± SEM.
Prearrest I = measurements before induction of cardiac arrest at normothermia, prearrest II = measurements before induction of cardiac arrest after hypothermia was achieved, Po_2 = oxygen partial pressure, ΔPco_2 (arterial/mixed venous) = arterial-mixed venous CO_2 gradient, ΔPco_2 (arterial/sagittal sinus) = arterial-sagittal sinus CO_2 gradient, ACD + ITV = active compression-decompression and impedance threshold valve, STD = standard compression.
* $P < 0.05$ ACD + ITV versus STD.

group during basic life support, although coronary perfusion pressure was comparable with STD CPR. This phenomenon may be explained by the observation of previous studies demonstrating that the relationship between perfusion pressure and blood flow is exponential rather than linear (23,24).

Because our recent results (14) demonstrated that vasopressin may be beneficial to improve coronary artery perfusion pressure in hypothermic animals, we chose to administer vasopressin in our study. Interestingly, we found coronary perfusion pressure to be significantly increased when vasopressin was administered during ACD CPR + ITV, whereas vasopressin was nearly ineffective during STD CPR. It has been speculated that vasopressor drugs given during hypothermic cardiac arrest may accumulate in the peripheral circulation (4) because external chest compressions may not effectively restore systemic circulation. Accordingly, we suggest that the drug effect of vasopressin was significantly greater with ACD CPR + ITV because of an improved systemic circulation compared with STD CPR. Vasopressin causes a pronounced blood flow shift from muscle, skin, and gut toward vital organs during CPR (25,26). Interestingly, common carotid artery blood flow was decreased after the administration of vasopressin in this study in both groups. Common carotid artery blood flow reflects both cerebral blood flow, and perfusion of the snout and skin of the head. Accordingly, we speculate that the administration of vasopressin may have significantly impaired blood flow in facial vessels, thus decreasing common carotid artery blood flow. Nevertheless, common carotid blood flow values after drug administration may now reflect cerebral blood flow more precisely. In addition, we found a lower arterial/sagittal sinus Pco_2 gradient in the ACD + ITV group which may also support our hypothesis of improved cerebral blood flow when mechanical devices are used for CPR.

Some limitations of the present study should be noted. These include different vasopressin receptors in pigs (lysine vasopressin) and humans (arginine vasopressin), which may result in a different hemodynamic response to exogenously administered arginine vasopressin. Second, the technique for measurement of common carotid blood flow used in this study results in values that may differ from absolute cerebral flow because of the rete mirabile, a flow-damping network of microarteries, which is interposed between the common carotid artery and the circle of Willis in

swine (27). Thus, carotid blood flow values reported for our pigs may be overestimated; however, this effect may be negligible because both groups were measured in the same manner.

In conclusion, during hypothermic cardiac arrest, ACD CPR with the ITV improved common carotid blood flow compared with STD CPR alone. Moreover, after the administration of vasopressin, coronary perfusion pressure was significantly higher during ACD CPR + ITV, but not during STD CPR.

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