Repeated Administration of Vasopressin but Not Epinephrine Maintains Coronary Perfusion Pressure After Early and Late Administration During Prolonged Cardiopulmonary Resuscitation in Pigs

Volker Wenzel, MD; Karl H. Lindner, MD; Anette C. Krismer, MD; Egfried A. Miller, BS; Wolfgang G. Voelckel, MD; Werner Lingnau, MD

Background—It is unknown whether repeated dosages of vasopressin or epinephrine given early or late during basic life support cardiopulmonary resuscitation (CPR) may be able to increase coronary perfusion pressure above a threshold between 20 and 30 mm Hg that renders defibrillation successful.

Methods and Results—After 4 minutes of cardiac arrest, followed by 3 minutes of basic life support CPR, 12 animals were randomly assigned to receive, every 5 minutes, either vasopressin (early vasopressin: 0.4, 0.4, and 0.8 U/kg, respectively; n=6) or epinephrine (early epinephrine: 45, 45, and 200 μg/kg, respectively; n=6). Another 12 animals were randomly allocated after 4 minutes of cardiac arrest, followed by 8 minutes of basic life support CPR, to receive, every 5 minutes, either vasopressin (late vasopressin: 0.4 and 0.8 U/kg, respectively; n=6), or epinephrine (late epinephrine: 45 and 200 μg/kg, respectively; n=6). Defibrillation was attempted after 22 minutes of cardiac arrest. Mean±SEM coronary perfusion pressure was significantly higher 90 seconds after early vasopressin compared with early epinephrine (50±4 versus 34±3 mm Hg, P,0.02; 42±5 versus 15±3 mm Hg, P<0.0008; and 37±5 versus 11±3 mm Hg, P<0.002, respectively). Mean±SEM coronary perfusion pressure was significantly higher 90 seconds after late vasopressin compared with late epinephrine (40±3 versus 22±4 mm Hg, P<0.004, and 32±4 versus 15±4 mm Hg, P<0.01, respectively). All vasopressin animals survived 60 minutes, whereas no epinephrine pig had return of spontaneous circulation (P<0.05).

Conclusions—Repeated administration of vasopressin but only the first epinephrine dose given early and late during basic life support CPR maintained coronary perfusion pressure above the threshold that is needed for successful defibrillation. (Circulation. 1999;99:1379-1384.)

Key Words: cardiopulmonary resuscitation ■ vasopressin ■ epinephrine ■ perfusion ■ drugs

The role of epinephrine during cardiopulmonary resuscitation (CPR) is currently controversial. In laboratory studies, epinephrine during CPR has been associated with an increase of myocardial oxygen consumption,1 ventricular arrhythmias,2 ventilation-perfusion defect,3 and more severe postresuscitation myocardial dysfunction.4 In clinical trials, epinephrine did not result in better outcome than did saline placebo.5 Furthermore, high-dose epinephrine was not able to improve hospital discharge rates.6–8

In laboratory investigations of cardiac arrest from either ventricular fibrillation9 or pulseless electrical activity,10 vasopressin provided more effective vital organ blood flow9,10 and cerebral oxygen delivery11 than did epinephrine. In preliminary clinical trials, vasopressin resulted in return of spontaneous circulation after unsuccessful prolonged advanced cardiac life support with epinephrine.12 Compared with epinephrine, vasopressin significantly improved 24-hour survival rate in a small (n=40) study of patients with ventricular fibrillation.13

Although the American Heart Association14 and the European Resuscitation Council15 recommend repeated administration of epinephrine during advanced cardiac life support, it is unknown whether epinephrine given repeatedly during CPR may be effective or whether this strategy may even result in inadvertent catecholamine toxicity. Moreover, it is unknown whether repeated administration of vasopressin...
Repeated Vasopressin vs Epinephrine During CPR

TABLE 1. Flow Chart of the Experimental Protocol

<table>
<thead>
<tr>
<th>Preparation, min</th>
<th>Cardiopulmonary Resuscitation, min</th>
<th>Postresuscitation Phase, min</th>
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<td>30†</td>
</tr>
<tr>
<td>60†</td>
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<td>60†</td>
</tr>
</tbody>
</table>

Early vasopressin vs early epinephrine: DA1† DA2† DA3
Late vasopressin vs late epinephrine: DA1† DA2†

†Defibrillation

VF indicates ventricular fibrillation; DA, drug administration. Early vasopressin vs early epinephrine: DA1, 0.4 U/kg vasopressin vs 45 μg/kg epinephrine; DA2, 0.4 U/kg vasopressin vs 45 μg/kg epinephrine; DA3, 0.8 U/kg vasopressin vs 200 μg/kg epinephrine. Late vasopressin vs late epinephrine: DA1, 0.4 U/kg vasopressin vs 45 μg/kg epinephrine; DA2, 0.8 U/kg vasopressin vs 200 μg/kg epinephrine.

*Sampling of blood gases, *measurement of hemodynamic variables.

during CPR is effective and whether such a treatment regimen may result in prolonged elevated systemic vascular resistance, which may induce cardiac failure in the postresuscitation phase. Furthermore, the effects of vasopressin versus epinephrine may vary significantly when given early or late during basic life support (BLS) CPR. Accordingly, the purpose of the present investigation was to evaluate the effects of repeated administration of optimal (0.4 U/kg) and high (0.8 U/kg) dosages of vasopressin versus optimal (45 μg/kg) and high (200 μg/kg) dosages of epinephrine in a porcine cardiac arrest model simulating a short (3 minutes) and prolonged (8 minutes) duration of BLS with subsequent advanced cardiac life support.

Methods

Surgical Preparation and Measurements

This study was performed according to Utstein-style guidelines16 on 24 healthy, 12- to 16-week-old swine (Tyrolean domestic pigs) of either sex weighing 30 to 40 kg. The animals were fasted overnight but had free access to water. The pigs were premedicated with azaperone (neuroleptic agent; 4 mg/kg IM) 1 hour before surgery, and anesthesia was induced with atropine (0.1 mg/kg IM) and 3% gelatin solution (4 mL kg IM) 1 hour before surgery, and anesthesia was induced with thiotepal (7 to 15 mg/kg IV). After intubation during spontaneous respiration, the pigs were ventilated with a volume-controlled ventilator (Draeger EV-A) with 100% O2 at 20 breaths per minute and with a tidal volume adjusted to maintain normocapnia. Anesthesia was maintained with propofol (6 to 8 mg · kg⁻¹ · h⁻¹) and a single dose of piritramide (30 mg). We achieved muscle paralysis with 8 mg pancuronium after intubation and subsequently with repeated doses of 8 mg pancuronium as needed. Ringer’s solution (6 mL · kg⁻¹ · h⁻¹) and a 3% gelatin solution (4 mL · kg⁻¹ · h⁻¹) were administered in the preparation phase before induction of cardiac arrest and in the postresuscitation phase. A standard lead II ECG was used to monitor cardiac rhythm; depth of anesthesia was judged according to blood pressure, heart rate, and electroencephalography (Neurotrac, Engström). If cardiovascular variables or electroencephalography indicated a reduced depth of anesthesia, we increased the propofol dose, and additional piritramide was given. Body temperature was maintained with a heating blanket between 38.0°C and 39.0°C.

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 measure cardiac output and to sample mixed venous blood. Cardiac output was measured with the thermodilution technique, and cardiac index was calculated by dividing cardiac output by body weight. Another 7F catheter was placed into the right atrium via femoral cutdown to measure right atrial pressure and for drug administration. Aortic, right atrial, and pulmonary artery pressures were measured with saline-filled catheters attached to pressure transducers (model 1290A, Hewlett Packard) 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). Coronary perfusion pressure (CPP) was defined as the difference between aortic and right atrial diastolic pressures. Blood gases were measured with a blood gas analyzer (Chiron Diagnostics), and end-tidal carbon dioxide was measured with an infrared absorption analyzer (Sirecust 960, Siemens).

Experimental Protocol

Fifteen minutes before cardiac arrest, 5000 U heparin IV was administered to prevent intracardiac clot formation, a single dose of 15 mg piritramide and 8 mg pancuronium was given, and hemodynamic parameters as well as blood gases were measured. A 50-Hz, 60-V alternating current was then applied via 2 subcutaneous needle electrodes to induce ventricular fibrillation. Cardiopulmonary arrest was defined as the point at which the aortic pressure decreased profoundly to hydrostatic pressure, and the ECG showed ventricular fibrillation; ventilation was stopped at that point. After 4 minutes of untreated ventricular fibrillation, closed-chest CPR was performed manually, and mechanical ventilation was resumed at the same setting as before induction of cardiac arrest. Chest compression, guided by acoustical auditones, was always performed by the same investigator at a rate of 80 compressions per minute. This investigator was blinded to hemodynamic and end-tidal carbon dioxide monitor tracings.

The first part of the study was designed to simulate administration of vasopressors after a short period of BLS CPR. Accordingly, after 4 minutes of ventricular fibrillation followed by 3 minutes of BLS CPR, 12 animals were randomly assigned to receive either vasopressin (early vasopressin group: 0.4, 0.4, and 0.8 U/kg; n=6) or epinephrine (early epinephrine group: 45, 45, and 200 μg/kg; n=6) or epinephrine (early epinephrine group: 45, 45, and 200 μg/kg; n=6) or epinephrine (late epinephrine group: 45, 45, and 200 μg/kg). Late vasopressin vs late epinephrine: DA1, 0.4 U/kg vasopressin vs 45 μg/kg epinephrine; DA2, 0.8 U/kg vasopressin vs 200 μg/kg epinephrine.

15 minutes before cardiac arrest, 5000 U heparin IV was administered to prevent intracardiac clot formation, a single dose of 15 mg piritramide and 8 mg pancuronium was given, and hemodynamic parameters as well as blood gases were measured. A 50-Hz, 60-V alternating current was then applied via 2 subcutaneous needle electrodes to induce ventricular fibrillation. Cardiopulmonary arrest was defined as the point at which the aortic pressure decreased profoundly to hydrostatic pressure, and the ECG showed ventricular fibrillation; ventilation was stopped at that point. After 4 minutes of untreated ventricular fibrillation, closed-chest CPR was performed manually, and mechanical ventilation was resumed at the same setting as before induction of cardiac arrest. Chest compression, guided by acoustical auditones, was always performed by the same investigator at a rate of 80 compressions per minute. This investigator was blinded to hemodynamic and end-tidal carbon dioxide monitor tracings.

All drugs were diluted to 10 mL with normal saline and subsequently injected into the right atrium, followed by 20 mL saline flush (investigators were blinded to the drugs). Hemodynamic parameters were measured before induction of cardiac arrest, after 3 minutes of CPR, and 90 seconds and 5 minutes after each drug administration, respectively. After 22 minutes of cardiac arrest, including 18 minutes of CPR, up to 5 countershocks were administered with an energy of 3, 4, and 6 J/kg. If asystole or pulseless electrical activity was present after defibrillation, the experiment was terminated. Return of spontaneous circulation was defined as an unassisted pulse with a systolic arterial pressure of ≥80 mm Hg and pulse pressure of ≥40 mm Hg lasting for at least 5 minutes. In the postresuscitation period,
hemodynamic parameters were measured at 5, 15, 30, and 60 minutes after return of spontaneous circulation. After the experimental protocol was finished, the animals were killed and necropsied to verify correct positioning of the catheters and injuries to the rib cage.

**Statistical Analysis**

The comparability of weight and baseline data were tested with the t test for continuous variables. One-way ANOVA was used to determine statistical significance between groups and was corrected for multiple comparisons by the Bonferroni method. Using Fisher’s exact test, we tested the null hypothesis that the number of surviving animals is independent of treatment. We considered a 2-tailed value of P<0.05 statistically significant.

**Results**

Before induction of ventricular fibrillation and before drug administration during CPR, there were no differences in weight, hemodynamic variables, or blood gases between groups (Table 2). When drugs were given early during BLS CPR (after 3 minutes of chest compressions), there was a strong trend toward significantly higher CPP 90 seconds after vasopressin compared with epinephrine. This trend became statistically significant between groups 5 minutes after the first vasopressin or epinephrine administration and remained significantly different for the remainder of the experiment (Figure 1).

When drugs were given late during BLS CPR (after 8 minutes of chest compressions), CPP was significantly higher after vasopressin compared with epinephrine at both 90 seconds and 5 minutes after each of 2 drug administrations (Figure 2). After 22 minutes of cardiac arrest, including 18 minutes of CPR, all pigs in the early and late vasopressin group had return of spontaneous circulation (early vasopressin group, 1.3±0.2 countershocks; late vasopressin group, 4.2±0.9 countershocks) and survived the 60-minute postresuscitation phase. In the early epinephrine group, 2 animals were defibrillated into pulseless electrical activity, and 4 animals had asystole. In the late epinephrine group, all animals had asystole. Necropsy confirmed appropriate catheter positions and revealed no injuries to the rib cage or intrathoracic organs in any animals.

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**TABLE 2. Hemodynamic Variables at Prearrest and After Return of Spontaneous Circulation (Postresuscitation Phase)**

<table>
<thead>
<tr>
<th></th>
<th>Prearrest</th>
<th>5</th>
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<tbody>
<tr>
<td>HR, bpm</td>
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<tr>
<td>Early vasopressin</td>
<td>90±5</td>
<td>133±16</td>
<td>129±17</td>
<td>148±12</td>
<td>155±16</td>
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<tr>
<td>Early epinephrine</td>
<td>100±1</td>
<td>...</td>
<td>...</td>
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</tr>
<tr>
<td>Late vasopressin</td>
<td>95±3</td>
<td>132±9</td>
<td>126±12</td>
<td>130±9</td>
<td>138±8</td>
</tr>
<tr>
<td>Late epinephrine</td>
<td>97±6</td>
<td>...</td>
<td>...</td>
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<tr>
<td>MAP, mm Hg</td>
<td></td>
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<tr>
<td>Early vasopressin</td>
<td>106±7</td>
<td>102±4</td>
<td>63±4</td>
<td>70±2</td>
<td>68±4</td>
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<td>Early epinephrine</td>
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<tr>
<td>Late vasopressin</td>
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<td>95±12</td>
<td>67±8</td>
<td>62±4</td>
<td>64±3</td>
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<tr>
<td>Late epinephrine</td>
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<tr>
<td>MPAP, mm Hg</td>
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<tr>
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<td>18±2</td>
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<td>19±2</td>
<td>22±2</td>
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<tr>
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<tr>
<td>Late vasopressin</td>
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<td>20±4</td>
<td>19±3</td>
<td>23±3</td>
<td>23±4</td>
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<tr>
<td>Late epinephrine</td>
<td>16±2</td>
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<td>...</td>
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<tr>
<td>CI, mL·kg⁻¹·min⁻¹</td>
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<tr>
<td>Early vasopressin</td>
<td>147±2</td>
<td>75±6</td>
<td>59±6</td>
<td>77±6</td>
<td>104±8</td>
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<tr>
<td>Early epinephrine</td>
<td>148±9</td>
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<tr>
<td>Late vasopressin</td>
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<td>94±21</td>
<td>58±15</td>
<td>87±13</td>
<td>123±10</td>
</tr>
<tr>
<td>Late epinephrine</td>
<td>146±8</td>
<td>...</td>
<td>...</td>
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<tr>
<td>SVR, dyne·s·cm⁻⁵</td>
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<tr>
<td>Early vasopressin</td>
<td>1604±85</td>
<td>3154±249</td>
<td>2263±159</td>
<td>1988±178</td>
<td>1361±122</td>
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<tr>
<td>Early epinephrine</td>
<td>1479±180</td>
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<tr>
<td>Late vasopressin</td>
<td>1601±181</td>
<td>2404±299</td>
<td>1831±181</td>
<td>1537±191</td>
<td>1115±169</td>
</tr>
<tr>
<td>Late epinephrine</td>
<td>1717±182</td>
<td>...</td>
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</table>

Prearrest indicates measurements before induction of cardiac arrest; postresuscitation phase, after return of spontaneous circulation; HR, heart rate; MAP, mean arterial pressure; MPAP, mean pulmonary arterial pressure; CI, cardiac index; SVR, systemic vascular resistance; . . ., not applicable—no return of spontaneous circulation; early vs late, first drug administration after 3 vs 8 minutes of basic life support CPR, respectively. Values are mean±SEM.
Repeated administration of vasopressin but only the first dose of epinephrine given early and late during BLS CPR were able to maintain CPP above the threshold between 20 and 30 mm Hg that is needed for successful defibrillation.22 Furthermore, these effects lasted longer after vasopressin than epinephrine, and significantly more vasopressin than epinephrine animals had return of spontaneous circulation (6 of 6 versus 0 of 6, respectively; \( P < 0.05 \)). The present model closely simulates a short and prolonged duration of BLS followed by advanced cardiac life support. Although the 45-\( \mu \)g/kg dose of epinephrine used in our porcine study is higher than the 15-\( \mu \)g/kg dose recommended for clinical use,14,15 the first dosages of both vasopressin and epinephrine reflect an established optimal dose in this pig model.9,17 Furthermore, the high doses of 0.8 U/kg vasopressin and 200 \( \mu \)g/kg epinephrine are the maximum effective doses in swine.9,18 Interestingly, the effects of vasopressin versus epinephrine on CPP varied depending on the time of drug administration during advanced life support CPR. For example, the first vasopressin administration in the late model achieved an \( \approx 66\% \) increase in CPP over the first vasopressin injection in the early model (~20 mm Hg versus 30 mm Hg). Conversely, the first epinephrine dose in the late model achieved only an \( \approx 35\% \) increase in CPP over the first epinephrine dose in the early model (~6 mm Hg versus \( \approx 17 \) mm Hg). This indicates that the effects of epinephrine given late seemed to be more attenuated compared with late administration of vasopressin during BLS CPR. In fact, arteries from rats with metabolic acidosis or uremia showed selective blunting of biochemical and contractile responses to norepinephrine but not to vasopressin.19 This may suggest that after prolonged cardiac arrest and therefore fundamental global hypoxia and hypercarbic acidosis, the pressor sensitivity to vasopressin may be normal and the effects of catecholamines may be blunted.10 The underlying mechanism for a rapid and profound tachyphylaxis of epinephrine may be desensitized myocardial and peripheral adrenergic receptors.20 Accordingly, substantially elevated plasma levels of epinephrine that are endogenously released immediately after cardiac arrest before initiation of CPR may be a possible explanation for limited effectiveness of epinephrine. This may explain that in addition to endogenous epinephrine, exogenous epinephrine is necessary to increase vital organ blood flow during CPR.21

A CPP between 20 and 30 mm Hg during CPR is one of the best predictors of return of spontaneous circulation in both animals and humans.22 The epinephrine animals reached this level only transiently 90 seconds after the first drug administration given early and late during BLS CPR, whereas CPP in the vasopressin animals was at or above this level for the entire experiment. Accordingly, all vasopressin animals in our study were successfully defibrillated after 22 minutes of cardiac arrest and survived the 60-minute postresuscitation phase, whereas all pigs resuscitated with epinephrine died. The duration of BLS and therefore of suboptimal vital organ blood flow during CPR may have a fundamental impact on resuscitability. For example, the early vasopressin pigs were successfully defibrillated with 1.3±0.2 countershocks, whereas the late vasopressin pigs needed 4.2±0.9 defibrillation attempts to achieve return of spontaneous circulation, indicating more severe cardiac ischemia.

Only the first of repeated doses of epinephrine in our animals were able to increase CPP above a threshold that renders successful defibrillation likely. Subsequent doses, including a high dosage, were not able to increase CPP above a level that usually correlates with return of spontaneous circulation. This is in good agreement with a preliminary canine study showing that the first dose of epinephrine determined whether the critical CPP needed for return of spontaneous circulation was reached and the animals survived.23 In fact, with the exception of 2 animals in the early epinephrine group that we defibrillated into pulseless electrical activity, all pigs treated with epinephrine had asystole, indicating fundamental depletion of myocardial energy. This
may confirm previous results from laboratory investigations demonstrating that epinephrine fueled cardiac oxygen consumption, which subsequently resulted in a severe mismatch of cardiac oxygen delivery versus oxygen consumption during CPR.

This mechanism may have been an important component in a clinical study, when a total cumulative dose of 15 mg epinephrine was found to best predict 24-hour component in a clinical study, when a total cumulative dose of arginine vasopressin, as administered in the present investigation, may be even greater in humans than in pigs. In addition, we did not evaluate vasopressin plasma levels throughout the study. Furthermore, we were not able to assess whether higher return of spontaneous circulation rates as observed in the early and late vasopressin animals might have had a beneficial effect on long-term survival and neurological outcome after return of spontaneous circulation. Also, usage of potent anesthetics may have impaired cardiovascular function and autonomic control. We also used young, healthy pigs that were free of atherosclerotic disease. Furthermore, this study lacks dose-response data; therefore, we are not able to report the minimally effective vasopressin dose. Finally, we purposely omitted defibrillation attempts on starting CPR and immediately after vasopressor administration to study the hemodynamic effects of the study drugs during the resuscitation attempt.

In conclusion, repeated administration of vasopressin but only the first epinephrine dose given early and late during BLS CPR maintained CPP above a threshold that is needed for successful defibrillation.

Acknowledgments

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References

6. Callaham M, Madsen CD, Barton CW, Saunders CE, Pointer J. A randomized clinical trial of high-dose epinephrine and norepinephrine vs...
standard-dose epinephrine in prehospital cardiac arrest. JAMA. 1992;268:
2667–2672.
7. Stiell IG, Hebert PC, Weititzman BN, Wells GA, Ramann S, Stark RM, 
Higgins LA, Ahuja J, Dickinson GE. High-dose epinephrine in adult 
8. Lindner KH, Ahnefeld FW, Prengel AW. A comparison of standard 
and high-dose adrenaline in the resuscitation of asystole and electrome-
9. Lindner KH, Prengel AW, Pfenninger EG, Lindner IM, Strohmenger HU, 
Georgieff M, Lurie KG. Vasopressin improves vital organ blood flow 
during closed-chest cardiopulmonary resuscitation in pigs. Circulation. 
10. Wenzel V, Lindner KH, Prengel AW, Maier C, Voeckel W, Lurie KG, 
Strohmenger HU. Vasopressin improves vital organ blood flow after 
prolonged cardiac arrest with post-countershock pulseless electrical 
11. Prengel AW, Lindner KH, Keller A. Cerebral oxygenation during car-
diopulmonary resuscitation with epinephrine and vasopressin in pigs. 
12. Lindner KH, Prengel AW, Brinkmann A, Strohmenger HU, Lindner IM, 
Lurie KG. Vasopressin administration in refractory cardiac arrest. Ann 
13. Lindner KH, Dirks B, Strohmenger HU, Prengel AW, Lindner IM, 
Lurie KG. A randomized comparison of epinephrine and vasopressin in 
14. Emergency Cardiac Care Committee and Subcommittees, American 
Heart Association. Guidelines for cardiopulmonary resuscitation, III: 
R, de Latorre DJ, Lindner K, Perales N. The European Resuscitation 
Council guidelines for adult advanced life support: a statement from the 
working group on advanced life support, and approved by the executive 
16. Idris AH, Becker LB, Ornato JP, Hedges JR, Bircher NG, Chandra NC, 
Cummins RO, Dick WF, Ebnmeyer U, Halperin HR, Hazinski MF, Kerber 
RE, Kern KB, Safar P, Steen PA, Swindle MM, Tistilic JE, von Planta I, 
von Planta M, Wears RL, Weil MH. Utstein-style guidelines for uniform 
17. Lindner KH, Ahnefeld FW, Bowdler IM. Comparison of different 
doses of epinephrine on myocardial perfusion and resuscitation success 
18. Brown CG, Werman HA, Davis EA, Hobson J, Hamlin RL. The effects 
of graded doses of epinephrine on regional myocardial blood flow during 
19. Fox AW, May RE, Mitch WE. Comparison of peptide and nonpeptide 
20. Insel PA. Adrenergic receptors: evolving concepts and clinical impli-
TJ, Feingold M, Cryer PE, Wortsman J, Nowak RM. The effect of 
standard- and high-dose epinephrine on coronary perfusion pressure 
during prolonged cardiopulmonary resuscitation. JAMA. 1991:265:
1139–1144.
22. Kern KB, Niemann JT. Coronary perfusion pressure during cardiopul-
Cardiac Arrest: The Science and Practice of Resuscitation Medicine. 
23. Cairns CB, Niemann JT. Hemodynamic effects of repeated doses of 
epinephrine after prolonged cardiac arrest and CPR: preliminary obser-
24. Ditchey RV. The choice of vasopressor agents in cardiopulmonary resus-
NM. The effect of the total cumulative epinephrine dose administered 
during human CPR on hemodynamic, oxygen transport, and utilization 
26. Kern KB, Ewy GA. Minimal coronary stenoses and left ventricular blood 
27. Reimer KA, Lowe JE, Rasmussen MM, Jennings RB. The wavefront 
phenomenon of ischemic cell death, I: myocardial infarct size vs duration 
28. Prengel AW, Lindner KH, Keller A, Lurie KG. Cardiovascular function 
during the postresuscitation phase after cardiac arrest in pigs: a com-
parison of epinephrine versus vasopressin. Crit Care Med. 1996;24:
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