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European Journal of Anaesthesiology / Volume 24 / Issue 07 / July 2007, pp 580 - 588

DOI: 10.1017/S0265021506002225, Published online: 23 January 2007

Link to this article: http://journals.cambridge.org/abstract_S0265021506002225

How to cite this article:

T. Palmaers, S. Albrecht, C. Leuthold, F. Heuser, J. Schuettler and B. Schmitz (2007). Post-resuscitation haemodynamics in a novel acute myocardial infarction cardiac arrest model in the pig. *European Journal of Anaesthesiology*, 24, pp 580-588
doi:10.1017/S0265021506002225

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Post-resuscitation haemodynamics in a novel acute myocardial infarction cardiac arrest model in the pig

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Summary

Background and objectives: Although a considerable amount of promising experimental research has been performed on cardiopulmonary resuscitation, clinical data indicate an ongoing limited outcome in human beings. One reason for this discrepancy could be that experimental studies use healthy animals whereas most human beings undergoing cardiopulmonary resuscitation suffer from acute or chronic myocardial dysfunction. To overcome this problem, we sought to develop a new model of myocardial infarction, that is easy to perform in all kind of laboratories and compromises on the myocardial function significantly. **Methods:** Following approval by the local authorities, 14 domestic pigs were instrumented for measurement of arterial, central venous, left atrial and left ventricular pressures. Myocardial infarction was induced in eight pigs by clipping the circumflex artery close to its origin from the left coronary artery (infarction group; $n = 8$). Six animals (no infarction group, $n = 6$) served as no-infarct controls. Following a 4-min period of cardiac arrest, internal cardiac massage was performed in these two groups, and haemodynamics were recorded during the first 30 min of reperfusion. **Results:** All animals were resuscitated successfully. Compared to the no-infarction group, the infarction group showed significantly decreased myocardial contractility, coronary perfusion pressure and cardiac index (30 min after restoration of spontaneous circulation: infarction group: 57 ± 7 and $89 \pm 19 \text{ mL min}^{-1} \text{ kg}^{-1}$ in the no-infarction group; mean $\pm$ SD; $P < 0.05$) during reperfusion. Two animals from the infarction group (25%), but none of the animals in the no-infarction group, died during the reperfusion period. **Conclusion:** These data demonstrate that clipping of the circumflex artery leads to a reduced myocardial performance after successful resuscitation, whereas the rate of restoration of spontaneous circulation is not reduced. Therefore, this set-up provides a reproducible model for future studies of post-resuscitation haemodynamics and treatment.

Keywords: HEART ARREST; CARDIOPULMONARY RESUSCITATION; MODELS, ANIMAL, pig; MYOCARDIAL INFARCTION; REPERFUSION INJURY.

Introduction

In the past, considerable experimental research has been performed on cardiac arrest and cardiopulmonary resuscitation (CPR). A wide range of different animal models such as mice, rats, cats, dogs and pigs have been used to gain insight into the mechanisms of successful CPR and post-resuscitation disorders [1–5].

Presented in part at the German Anaesthesia Congress (DAC 2004) June 2004, Nuremberg, Germany and at the Congress of the European Society of Anaesthesiology (ESA 2004), May 2004, Lisbon, Portugal.

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Accepted for publication 27 September 2006 EJA 3917
First published online 23 January 2007

Using these models, pharmacological interventions [6–10] and therapeutic strategies [11–13] have been developed to improve resuscitation rates and neurological outcomes following cardiac arrest and CPR. However, despite tremendous knowledge obtained in experimental studies, clinical data collected over the past decade indicate an ongoing limited outcome in cardiac arrest victims [14–21].

A possible explanation for this discrepancy could be different pre- and post-arrest conditions of young and healthy experimental animals and human beings with pre-existing cardiac disease suffering from cardiac arrest. This is underlined by the fact that investigations on the aetiology of cardiac arrest in human beings showed that up to 75% were of cardiac origin [22–25]. Nevertheless, most animal models have ignored the importance of coronary obstruction resulting in profound effects on CPR physiology [26,27], which may lead to unsuccessful resuscitation efforts or secondary cardiac decompensation and cardiac arrest despite primarily successful CPR.

Therefore, the purpose of our investigation was to develop a model of acute myocardial infarction induced cardiac arrest in pigs. The model should be easy to perform and not require special and sophisticated cardiology laboratory equipment. Myocardial performance should be considerably impaired, indicating relevant acute myocardial damage without rendering CPR impossible, thus making it possible to study post-resuscitation haemodynamics and treatment. In this paper, we describe the model and the haemodynamic consequences of acute myocardial infarction on the early reperfusion period following successful CPR.

Methods

This study and the experimental protocol have been approved by the animal investigation committee of the local authorities, and were conducted according to the German legislation on animal care (Regierung von Mittelfranken 621-2531.31-2/01).

A random list was generated with sealed envelopes. From this list, the animals were assigned to one of the two experimental groups (infarction and no-infarction group).

Fourteen domestic pigs, weighing 26–32 kg and of either sex, were fasted overnight except for water that was allowed *ad libitum*. All animals were clinically normal and free of disease. The animals were premedicated with atropine 0.5 mg, midazolam 0.5 mg kg⁻¹ and ketamine 15 mg kg⁻¹, which were administered intramuscularly.

After placement of an intravenous (i.v.) line on the back of the right ear, the animals received a

basic infusion of Ringer's solution (10 mg kg⁻¹ h⁻¹). Subsequently, propofol 2 mg kg⁻¹ were injected, and the pigs were intubated orotracheally with a 7 mm (ID) endotracheal tube. Following intubation, pancuronium 0.2 mg kg⁻¹ and fentanyl 30 µg kg⁻¹ were given i.v. Anaesthesia was maintained by continuous i.v. administration of propofol 8 mg kg⁻¹ h⁻¹, pancuronium 0.1 mg kg⁻¹ h⁻¹ and fentanyl 20 µg kg⁻¹ h⁻¹.

Volume-controlled mechanical ventilation (Servo 300 Ventilator; Siemens AG, Erlangen, Germany) was performed with 30% oxygen in air, a respiratory rate of 20 min⁻¹ and tidal volumes of 8–10 mL kg⁻¹ to keep end-tidal CO₂ at 35–40 mmHg.

Standard monitoring included a 5-lead electrocardiogram, pulse-oxymetric measurement of the oxygen saturation and end-tidal CO₂ (Sirecust 1084, Siemens AG, Erlangen, Germany).

The animals were then brought into the supine position, and all preparations and catheter placements were performed under surgical conditions. A 7-Fr 30 cm double-lumen catheter (Arrow International Inc., Reading, PA, USA) was inserted into the right femoral artery, and slid forward to the descending aorta until its tip was positioned above the diaphragm (correct positioning was verified fluoroscopically). This catheter was used for collection of blood samples (blood gas analysis) and measurement of mean and diastolic aortic pressure. A 7-Fr triple-lumen catheter (Arrow International Inc.) was inserted via the right internal jugular vein (correct position was verified fluoroscopically) for measurement of the end diastolic right atrial pressure and drug administration. Following a median thoracotomy, the pericardium was opened. A 7-Fr thermistor catheter (Arrow International Inc.) was placed directly into the pulmonary artery in order to measure cardiac output using the thermodilution technique. A 4-Fr single lumen catheter (Arrow International Inc.) was placed into the left atrium for measurement of left atrial pressure. Another 4-Fr single lumen catheter (Arrow International Inc.) was inserted into the left ventricle to measure left ventricular pressure via the apex of the left ventricle. All three catheters (pulmonary artery catheter, left atrial catheter and left ventricular catheter) were fixed by tobacco-pouch sutures, and their correct position was verified by autopsy after the experiment. All pressures were monitored (Sirecust 1281; Siemens AG, Erlangen, Germany), using high-fidelity pressure transducers (Smith Medical, Kirchseeon, Germany), calibrated to the right atrial level. Coronary perfusion pressure was defined as the aortic diastolic pressure minus right atrial diastolic pressure [26]. Cardiac output was measured in triplicate by the thermodilution technique (three

single measurements, each with a bolus of 10 mL of Ringer's solution (5–10°C), were performed and the results averaged). The calculation of cardiac index was performed by dividing cardiac output and body weight, since there is no quotation to calculate the body surface area of pigs and this method has been widely used in pig resuscitation models [28]. To prevent intra-cardiac clot formation, the animals received heparin (125 IU kg⁻¹) prior to induction of cardiac arrest. Core temperature was measured in the pulmonary artery and was kept at 37–38°C.

Following surgical preparation, baseline conditions were allowed to stabilize for 20 min. Then, ventricular fibrillation was induced by a 9 V direct current applied for 15–20 s to the surface of the left ventricle. Cessation of cardiac action and a drop of systolic arterial pressure below 25 mmHg confirmed cardiac arrest. Artificial ventilation, drug administration and fluid infusions were stopped. In the infarction group, the circumflex artery was exposed and clipped close to its origin from the left coronary artery to produce myocardial infarction (infarction group, $n = 8$). Six animals served as no-infarcted controls and underwent the same CPR protocol.

After 4 min of untreated ventricular fibrillation, CPR was performed by an open-chest cardiac massage at a rate of about 100 min⁻¹, artificial ventilation with 100% oxygen and epinephrine given i.v. at a dose of 30 µg kg⁻¹. In all experiments, open-chest cardiac massage was performed by the same investigator, who was blinded to the haemodynamic measurements during CPR. Success of his cardiac massage was confirmed by taking the femoral pulse.

After 1 min of cardiac massage, a maximum of three internal defibrillations (1 J kg⁻¹) (Siemens, Theracard 361D, Siemens AG, Germany) were applied and repeated after 60 s, if necessary. If this failed to restore spontaneous circulation, an additional dose of epinephrine (15 µg kg⁻¹) was given i.v., cardiac massage was continued for 3 min, and a further series of defibrillations (1.5 J kg⁻¹) was applied. This cycle was repeated, if necessary, and CPR was considered unsuccessful if spontaneous circulation could not be restored within 20 min. Return of spontaneous circulation (ROSC) was defined as spontaneous cardiac action with a mean arterial pressure of above 50 mmHg for at least 3 min.

After ROSC, the i.v. fluid therapy was resumed and anaesthetics were restarted. Mechanical ventilation was provided with 100% oxygen and adjusted to obtain an end-tidal CO₂ of 35–40 mmHg. No attempts were made to support cardiac function or to correct acidosis during recirculation. Thirty minutes after ROSC, the experiment was terminated by the induction of ventricular fibrillation

and an autopsy was performed to verify the correct position of all catheters.

Infarction size was determined by excising the heart and injecting cardiogreen (0.5 mg mL⁻¹) (ICG-Pulsion; Pulsion AG, Munich, Germany) into the right and left coronary artery. Perfused myocardial tissue changed its colour to green. Not-perfused tissue remained normal with exact demarcation lines of the infarction area. After this procedure, the left ventricle was excised from the rest of the heart and weighed. Then, the not-perfused (not green) tissue was excised from the left ventricle, weighed and related to the mass of the whole left ventricle.

Measurements and data collection

Haemodynamic variables were recorded with exception of the left ventricular pressure curve at *a priori* defined time-points (baseline controls before CPR, ROSC + 1 min, ROSC + 4 min, ROSC + 8 min, ROSC + 15 min, ROSC + 20 min and ROSC + 30 min) and documented in a database. Left ventricular pressures were recorded continuously, digitized and stored on a PC (DasyLab 3.5, DataLog, Mönchengladbach, Germany). Left ventricular contractility was determined by calculation of the maximal rate of left ventricular pressure increase over time (dP/dt_{max}).

Statistical analysis

All variables were tested for normality, using Shapiro–Wilk test. All normally distributed data are expressed as mean ± SD, and not normally distributed data are expressed as mean ± interquartile range. Only once determined data was tested for statistical differences using paired *t*-test, if normally distributed, and *U*-test, if not normally distributed. Data collected more than once were tested using ANOVA with Fisher's LSD test and Bonferroni's test for multiple comparisons for *post hoc* testing. A probability value of $P < 0.05$ was considered significant. All tests were performed with Statistika 6.0 (StatSoft, Tulsa, OK, USA).

Results

Before cardiac arrest, the physiological variables were within the normal range, and there were no differences in baseline data between infarction and no-infarction group (Tables 1 and 2).

Induction of ventricular fibrillation caused instantaneous cessation of cardiac action and a drop of systolic pressure below 25 mmHg. Clipping of the circumflex artery was performed in all animals in less than 30 s. All animals could be resuscitated

Table 1. Comparison of the INF ($n = 8$) and the NOINF ($n = 6$) group in their differences at baseline and during resuscitation.

	INF ($n = 8$)	NOINF ($n = 6$)
Weight (kg)	28 ± 3	31 ± 3
Defibrillations needed (n)	$7 \pm [4-13]$	$2 \pm [1-5]$
Peak MAP during CPR (mmHg)	90 ± 36	73 ± 11
Peak MAP after ROSC (mmHg)	$171 \pm 32^*$	$210 \pm 34^*$
Cumulative epinephrine dose (mg)	$0.9 \pm [0.8-1.3]$	$0.9 \pm [0.9-0.9]$
Duration of CPR (s)	$105 \pm [93-270]$	$75 \pm [70-123]$

Normally distributed data is presented as mean $\pm$ SD; not normally distributed data is presented as median $\pm$ [25%/75% interquartile range]. INF: infarction; NOINF: no infarction. * $P < 0.05$.

Table 2. Haemodynamic variables before (T0) and after resuscitation (ROSC+1, 4, 8, 15, 20 and 30 min).

	Pre-arrest T(0)	ROSC + 1 min T(1)	ROSC + 4 min T(4)	ROSC + 8 min T(8)	ROSC + 15 min T(15)	ROSC + 20 min T(20)	ROSC + 30 min T(30)
Heart rate (min^{-1})							
INF, $n = 8/6$	95 ± 10	$217 \pm 26^*$	$193 \pm 22^*$	$175 \pm 29^*$	$149 \pm 34^*$	135 ± 43	136 ± 38
NOINF, $n = 6$	99 ± 9	$193 \pm 57^*$	$175 \pm 25^*$	$158 \pm 20^*$	$137 \pm 13^*$	$130 \pm 20^*$	$133 \pm 25^*$
MAP (mmHg) [#]							
INF, $n = 8/6$	100 ± 14	$160 \pm 33^*$	129 ± 40	106 ± 35	70 ± 33	$51 \pm 26^*$	$61 \pm 19^*$
NOINF, $n = 6$	103 ± 11	$173 \pm 62^*$	$141 \pm 11^*$	$120 \pm 8^*$	90 ± 14	$83 \pm 15^{\#}$	83 ± 17
RAEDP (mmHg)							
INF, $n = 8/6$	5 ± 2	$11 \pm 2^*$	9 ± 3	8 ± 4	7 ± 3	7 ± 3	7 ± 3
NOINF, $n = 6$	7 ± 2	11 ± 3	8 ± 1	7 ± 2	6 ± 2	6 ± 2	6 ± 1
Mean LAP (mmHg) [#]							
INF, $n = 8/6$	9 ± 2	$40 \pm 15^*$	$29 \pm 14^*$	$21 \pm 9^*$	18 ± 9	$18 \pm 6^*$	$19 \pm 5^*$
NOINF, $n = 6$	15 ± 7	$41 \pm 14^*$	18 ± 7	16 ± 5	14 ± 3	12 ± 3	$11 \pm 2^{\#}$
LVSP (mmHg) [#]							
INF, $n = 8/6$	105 ± 11	$177 \pm 41^*$	135 ± 30	114 ± 25	81 ± 29	$63 \pm 19^*$	$69 \pm 17^*$
NOINF, $n = 6$	103 ± 7	$189 \pm 40^*$	$148 \pm 14^*$	$123 \pm 10^*$	99 ± 13	$97 \pm 20^{\#}$	$94 \pm 25^{\#}$

The normal distributed values are presented as mean $\pm$ SD; INF group ($n = 8$, T0–T8 and $n = 6$, T15 and T30, as two animals died in this group after 12 and 13 min); NOINF, control group ($n = 6$; T0–T30) without myocardial infarction ($n = 6$). MAP: mean arterial pressure; RAEDP: right atrial end diastolic pressure; LAP: left atrial pressure; LVSP: left ventricular systolic pressure; INF: group with myocardial infarction; NOINF: no infarction; ROSC: return of spontaneous circulation.

[#]Indicates a significant difference ($P < 0.05$) between the two groups; * indicates a significant difference from T0 ($P < 0.05$).

successfully. Return of spontaneous circulation was achieved within 105 (93–270)s in the infarction group and 75 (70–123)s in the no-infarction group (not significant). However, two of eight (25%) animals in the infarction group died after 12 and 13 min of recirculation, respectively, due to progressive myocardial failure. No further resuscitation attempt was made on these animals. The number of defibrillations required for termination of ventricular fibrillation ($7 \pm (4-13)$ vs. $2 \pm (1-5)$; not significant) and the cumulative epinephrine dose (39.7 ± 5.9 vs. $29.7 \pm 0.3 \mu\text{g kg}^{-1}$; not significant) tended to be higher in the infarcted animals.

Return of spontaneous circulation was followed by an immediate and sharp rise of mean arterial pressure (MAP), which peaked at 210 ± 34 mmHg in the no-infarction group and 171 ± 32 mmHg in the infarction group ($P < 0.05$). During the entire

observation period, a trend to higher MAP and left ventricular pressures was observed in the no-infarction group, and after 20 min these differences between the two groups became significant (Table 2). In contrast to the infarction group, MAP and left ventricular pressure stabilized at pre-arrest levels in the no-infarction group, whereas in the infarction group, they were significantly lower as compared to control at 20 and 30 min of reperfusion ($P < 0.05$).

Compared to baseline, left atrial pressure was significantly elevated in both groups by 1 min of recirculation, but in contrast to the infarction group, it returned rapidly to control level in the no-infarction group. The difference between the groups became significant after 30 min of reperfusion (Table 2).

Compared to baseline, myocardial contractility increased significantly 1 min after return of spontaneous circulation in both groups ($193 \pm 17\%$ and

Figure 1.

Time course of dP/dt_{max} . Myocardial contractility (dP/dt_{max} in mmHg s^{-1}) at baseline and different time points (+ min) following ROSC. Data presented as mean $\pm$ SD. Note significant differences between groups by 20 and 30 min of reperfusion. * Indicates a significant difference from baseline ($P < 0.05$). # Indicates a significant difference from the INF ($P < 0.05$). ROSC: Return of spontaneous circulation.

Figure 2.

Time course of cardiac index. Cardiac index at baseline and different time points (+ min) following ROSC. Data presented as mean $\pm$ SD. Note significant differences between groups by 15, 20 and 30 min of reperfusion. * Indicates a significant difference from baseline ($P < 0.05$). # Indicates a significant difference from the INF ($P < 0.05$). ROSC: Return of spontaneous circulation.

$238 \pm 24\%$ of control, respectively). But while it stabilized at pre-arrest level in no-infarcted animals, a progressive and significant decline in the infarction group was observed (up to $59.5 \pm 7.9\%$ of control). In the infarction group, myocardial contractility was significantly different from the no-infarction group at 20 and 30 min of reperfusion (Fig. 1).

While cardiac index remained almost stable in the no-infarction group (except for ROSC +

30 min: $74.4 \pm 5.0\%$), a progressive and significant decline was seen in infarcted animals (up to $44.3 \pm 1.8\%$ of control at 30 min), indicating a severe low cardiac output syndrome in the infarction group. After 15 min, differences between the groups became significant (Fig. 2).

After a significant increase of coronary perfusion pressure 1 min after ROSC in both groups, there was a further decrease in both groups. However, after 15, 20 and 30 min, the infarction group

Figure 3.

Time course of coronary perfusion pressure. Coronary perfusion pressure at baseline and different time points (+min) following ROSC. Data presented as mean $\pm$ SD. Note significant differences between groups by 15, 20 and 30 min of reperfusion. *Indicates a significant difference from baseline ($P < 0.05$). #Indicates a significant difference from the INF ($P < 0.05$). ROSC: Return of spontaneous circulation.

showed significantly lower coronary perfusion pressure values compared to the baseline and the no-infarction group (Fig. 3).

Infarction size in the infarction group animals was $39 \pm 5\%$ of the left ventricle.

Discussion

The results of the present study clearly demonstrate the feasibility of experimental CPR research, using a new model of acute coronary occlusion and subsequent myocardial infarction. However, the vast majority of experimental CPR research has been performed in animals without acute or chronic myocardial dysfunction, which may lead to problems in transferring the results of these experiments to the pre-clinical setting.

Cardiovascular physiology and coronary anatomy of pigs are closer to those of human beings than in other no-primate species [29,30]. Especially, the lack of collateral coronary circulation makes the pig a more suitable model of acute coronary obstruction, which more accurately resembles human anatomy than the dogs [31]. By clipping the circumflex artery close to its origin from the left coronary artery, we were able to create reproducible myocardial infarction of constant size, resulting in a significant reduction of myocardial performance in the early post-resuscitation period.

There are previous reports of CPR following acute myocardial infarction in pigs, induced by using transcatheter techniques to occlude the left

anterior descending coronary artery [26,32]. As this very elegant technique allows the use of standard closed chest compressions during CPR, our decision to use an open-chest model deserves discussion. First, the placement of an occluding cylinder by transcatheter techniques requires equipment to perform coronary angiography, which is not available in all experimental laboratories. Moreover, Berg and colleagues [32] had to exclude 12% of the animals from further experimentation owing to problems during coronary artery occlusion. Secondly, our experimental set-up presumes extensive cardiovascular instrumentation for measurement of several invasive pressures. In our experience, extensive invasive monitoring in the pig closed-chest CPR model leads to refractory ventricular fibrillation in an unacceptable proportion of animals, thus excluding this approach.

In preliminary investigations, we searched the ideal position for the ligation of a coronary artery to produce myocardial infarction. In five animals, we clipped the left anterior descending artery directly behind the first diagonal branch. Sixty percent of these animals were not successfully resuscitated owing to therapy-resistant ventricular fibrillation. This is in line with the results of Berg and colleagues [32], who found a similarly low rate of ROSC (53–64%) and high mortality rate during the observation period following occlusion of the left anterior descending artery (LAD). In an open-chest CPR setting, DeBehnke and colleagues [31] were unable to successfully resuscitate 33% of infarcted

dogs following LAD obstruction. In contrast, by clipping of the circumflex artery, we were able to produce an acute myocardial infarction, with significant depression of myocardial function and 100% ROSC. In view of these facts, the mortality of two animals during early reperfusion seems to be acceptable. We know well about the limitations of open-heart CPR, especially the difficulty of transferring CPR results to the pre-clinical setting. However, DeBehnke and colleagues [31] have published a detailed comparison of standard external CPR, open-chest CPR and cardiopulmonary bypass. Despite a significantly higher coronary perfusion pressure during CPR in the open-chest and the bypass groups compared to standard CPR, these authors found no significant differences between groups regarding haemodynamic data or arterial blood gases during the post-resuscitation period. As we focused on exactly this period and did not aim at improving ROSC, we think that for the assessment of post-CPR haemodynamics, it remains a suitable model.

Another particular point of our model is that we induced ventricular fibrillation first and then clipped the circumflex artery. In pilot experiments, we tried to clip first and then induced ventricular fibrillation, being more closed to the clinical situation. Unfortunately, the complication rate was extremely high, with a great proportion of animals starting to fibrillate while preparation was not yet finished, and others bleeding during the preparation of the circumflex artery owing to technical problems evoked by the beating heart. In order to prevent inhomogeneous groups with respect to duration of fibrillation, duration of myocardial infarction before cardiac arrest and bleeding complications, we decided to induce ventricular fibrillation first and then clip the circumflex artery, leading to exactly 4 min of cardiac arrest and no bleeding complication.

We observed a trend to prolonged and more difficult CPR, as indicated by cumulative epinephrine dose, duration of CPR and number of defibrillations in the infarction group, emphasizing increased severity of myocardial ischaemic injury with subsequently augmented likelihood of ectopic ventricular arrhythmias. These differences may have reached statistical significance with a larger number of experiments, but as the study did not focus on the CPR period itself, this lack of significance seems to be acceptable.

In the first 4 min following ROSC, haemodynamic variables in both groups exceeded by far the pre-arrest values, which is in line with earlier observations [8,33,34], and this can be attributed to the α - and β -adrenergic properties of epinephrine. Interestingly, cardiac index remained almost

unchanged compared to control, which may be attributed to severe tachycardia during this phase, preventing sufficient left ventricular filling during diastole and reduced post-ischaemic left-ventricular compliance, which is underlined by concomitant severely increased left atrial end-diastolic pressures.

Analysis of haemodynamic measurements revealed a catecholamine-induced striking increase immediately following ROSC. However, the parallel three- to fourfold increase in left atrial pressure indicates severe post-ischaemic myocardial dysfunction.

With ongoing reperfusion, haemodynamics returned to pre-arrest values in the no-infarction group, where only cardiac index showed a significant but even moderate reduction (-26%) by 30 min following ROSC as compared to pre-arrest. This observation is in line with the results of Gazmuri and colleagues [35], who described a reduction in cardiac index of about 20% by 30 min of reperfusion, whereas Lindner and colleagues [36] described a reduction of -21% , and Prengel and colleagues [28] (-17%) at the same time. Additionally, in the no-infarction group, we did not find significantly lower coronary perfusion pressure values at any time point compared to the baseline. This finding is in line with the results of Lindner and colleagues [36] and Prengel and colleagues [28]. In contrast to this observation, the infarction group showed significantly reduced coronary perfusion pressure levels compared to the baseline and the no-infarction group. Moreover, of note is that in the no-infarction group, myocardial contractility was at no time point lower than at baseline and mean left atrial pressure normalized within the first 4 min of reperfusion, indicating rapid recovery of myocardial performance. In contrast, in the infarction group, mean left atrial pressure remained elevated throughout the observation period and myocardial performance, as indicated by cardiac index and contractility measurements, was severely depressed during the second half of the reperfusion phase.

However, there are some limitations of the study. As mentioned above, we performed an open-heart resuscitation, which is certainly not the standard procedure during cardiac arrest. However, this open-chest model facilitates the determination of many invasive pressures as well as produces the wanted artificial myocardial infarction by clipping the circumflex coronary artery. Moreover, the short observation period without 24 h outcome, and the lack of the determination of vital organ blood flows, do not allow to predict differences in the long term and the functional outcome and will have to be addressed in future studies.

In summary, these experiments clearly demonstrate that acute myocardial infarction in pigs

significantly impairs myocardial performance during the early post-resuscitation phase. Technically, easy clipping of the circumflex artery resulted in greater mortality in the infarction group during reperfusion, while CPR attempts were successful in all animals. Therefore, the use of the model described here may be recommended for future CPR investigations for comparing different drug treatment strategies with respect to haemodynamic differences during reperfusion.

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