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The critical importance of minimal delay between chest compressions and subsequent defibrillation: a haemodynamic explanation

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Abstract

Outcome after prehospital defibrillation remains dire. The aim of the present study was to elucidate the pathophysiology of cardiac arrest and to suggest ways to improve outcome. Ventricular fibrillation (VF) was induced in air-ventilated pigs, after which ventilation was withdrawn. After 6.5 min of VF, ventilation with 100% oxygen was initiated. In six pigs (group I), defibrillation was the only treatment carried out. In another six pigs (group II), mechanical chest compression–decompression CPR (mCPR) was carried out for 3.5 min followed by a 40-s hands-off period before defibrillation. If unsuccessful, mCPR was resumed for a further 30 s before a second or a third, 40-s delayed, shock was given. In a final six pigs (group III) mCPR was applied for 3.5 min after which up to three shocks (if needed) were given during on-going mCPR. Return of spontaneous circulation (ROSC) occurred in none of the pigs in group I (0%), in 1 of six pigs in group II (17%) and in five of six pigs in group III (83%). During the first 3 min of VF arterial blood was transported to the venous circulation, with the consequence that the left ventricle emptied and the right ventricle became greatly distended. It took 2 min of mCPR to establish an adequate coronary perfusion pressure, which was lost when the mCPR was interrupted. During 30 s of mCPR coronary perfusion pressure was negative, but a carotid flow of about 25% of basal value was obtained. In this pig model, VF caused venous congestion, an empty left heart, and a greatly distended right heart within 3 min. Adequate heart massage before and during defibrillation greatly improved the likelihood of return of spontaneous circulation (ROSC).

Keywords: Active compression–decompression; Non-interrupted CPR; CPR before defibrillation; Coronary perfusion pressure; Return of spontaneous circulation; LUCAS

Resumo

O resultado após desfibrilhação pré-hospitalar continua mau. O presente estudo teve por objectivo esclarecer a patofisiologia da paragem cardíaca e sugerir formas de melhorar o prognóstico. Foi induzida fibrilhação ventricular (FV) em porcos ventilados com ar, após o que foi suspensa a ventilação. Ao fim de 6.5 min de FV iniciou-se ventilação com oxigénio a 100%. Em 6 porcos (grupo I), a desfibrilhação foi o único tratamento efectuado. Noutros 6 porcos (grupo II) fez-se reanimação cardiopulmonar com compressão-descompressão mecânica do tórax (mRCP) durante 3.5 min, seguido de uma pausa de 40 segundos antes da desfibrilhação. Se não houvesse sucesso, a mRCP era retomada durante mais 30 segundos antes de administrar um segundo ou terceiro choque, precedido de uma pausa de 40 segundos. No último grupo de 6 porcos (grupo III) foi feita mRCP durante 3.5 min, após o que eram administrados até 3 choques (se necessário) sem paragem da mRCP. Não houve recuperação da circulação espontânea (ROSC) em nenhum dos porcos do grupo I (0%), mas conseguiu-se ROSC em 1 de 6 porcos do grupo II (17%) e em 5 de 6 porcos do grupo III (83%). Verificou-se que nos primeiros 3 minutos de FV o sangue arterial era desviado para a circulação venosa, com o consequente do esvaziamento do ventrículo esquerdo o que decorria a par da constatação de que o ventrículo direito ficava largamente distendido. A pressão de perfusão coronária adequada, que se perdia quando era interrompida a mRCP, só se restabeleceu ao fim de 2 minutos de mRCP. A pressão de perfusão coronária era negativa durante os 30 segundos de mRCP, mas obteve-se um fluxo

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carotídeo de cerca de 25% do valor basal. Neste modelo em porcos, a FV provocou congestão venosa, um coração esquerdo vazio e um coração direito largamente distendido em 3 minutos. A massagem cardíaca adequada antes e durante a desfibrilhação aumentou grandemente a probabilidade de ROSC.

Palavras chave: Compressão-descompressão activa; RCP contínua; RCP antes de desfibrilhação; Pressão de perfusão coronária; Recuperação da circulação espontânea (ROSC); LUCAS

Resumen

El resultado después de desfibrilación prehospitalario sigue siendo espantoso. El objetivo de este estudio fue elucidar la fisiopatología del paro cardiaco y los métodos sugeridos para mejorar los resultados. Se indujo fibrilación ventricular (VF) en cerdos ventilados con aire, después de lo cual se suprimió la ventilación. Después de 6.5 minutos de VF, se inició ventilación con 100% de oxigeno. En 6 cerdos (grupo I), la desfibrilación fue el único tratamiento realizado. En otros 6 cerdos (grupo II), se realizó reanimación cardiopulmonar con compresión y descompresión mecánica (mCPR) por 3.5 minutos seguidos de 40 segundos sin compresión antes de la desfibrilación. Si no es exitosa, se reasume por los siguientes 30 segundos antes de dar una segunda o un tercera descarga, retrasada 40 segundos. En un grupo final de 6 cerdos (grupo III) se aplicó mCPR por 3.5 minutos después de lo cual se entregaron hasta tres descargas (si fueron necesarias) durante la reanimación que se llevaba a cabo.Ocurrió retorno a circulación espontánea (ROSC) ocurrió en ninguno de los cerdos del grupo I (0%), en 1 de los 6 en el grupo II (17%) y en 5 de 6 del grupo III (83%). Durante los 3 primeros minutos de VF la sangre arterial fue transportada a la circulación venosa, con la consecuencia del vaciamiento del ventrículo izquierdo y el ventrículo derecho se distendió ampliamente. Requirió 2 minutos de mCPR para establecer una presión de perfusión coronaria adecuada, la que se perdió cuando se interrumpió la mCPR. Durante 30 segundos de mCPR la presión de perfusión coronaria fue negativa, pero se obtuvo un flujo carotídeo de cerca de 25% del valor basal.En este modelo porcino, la VF causó una congestión venosa, un corazón izquierdo vacío, y un ventrículo derecho muy distendido dentro de 3 minutos. Un masaje cardíaco adecuado antes y durante la desfibrilación mejoró ampliamente la posibilidad de ROSC.

Palabras clave: RCP compresión descompresión activa; RCP no interrumpida; RCP antes de desfibrilar; Presión de perfusión coronaria; Retorno a circulación espontánea (RCE); Resucitación intrahospitalaria LUCAS

1. Introduction

Outcome after pre-hospital defibrillation remains dire. Recent evidence, however, has shown that in cases of cardiac arrest that have lasted more than 4 min, outcome can be improved if chest compressions are performed before any attempt at defibrillation [1,2].

The aim of the present investigation was to elucidate three issues. First, why is it so difficult to achieve return of spontaneous circulation (ROSC) after more than 4 min of ventricular fibrillation (VF) cardiac arrest? Second, why is it apparently important to give chest compressions before defibrillation if VF has lasted more than 4 min? Third, what pathophysiological changes occur, that negatively affect ROSC, if chest compressions are interrupted before defibrillation attempts?

We used a porcine model to investigate these issues, and the experiments were designed according to the Utstein guidelines for experimental studies of cardiopulmonary resuscitation (CPR) [3].

2. Materials and methods

We have recently described in detail our experimental method for porcine CPR experiments [4]. The same methods were used and only additional information that is specific to the present study is given here.

2.1. Experimental animals

Twenty-four Swedish domestic pigs with a mean weight of 22 kg (range 20–25 kg) were used. Eighteen of the pigs were randomized into three treatment groups. In addition, three pigs were used for video filming of the fibrillating heart and three pigs for intrapericardial pressure measurements before and during VF.

All the animals received humane care in compliance with the Guide for the Care and Use of Laboratory Animals, published by the National Institutes of Health (NIH publication 85-23, revised 1985). The study was approved by the ethical committee for animal experiments at the University of Lund, Sweden.

2.2. Anaesthesia, ventilation, and haemodynamic measurements

Anaesthesia was induced with one dose of intramuscular ketamine (30 mg/kg). Before tracheotomy, sodium thiopental (5–8 mg/kg) and atropine (0.02 mg/kg) were given intravenously. Anaesthesia and muscular paralysis were maintained with a continuous infusion of 30 ml per hour of a 10% glucose solution containing ketamine (16 mg/ml) and pancuronium (0.6 mg/ml). The animals were kept normothermic by a heating system in the operation table.

Pressure regulated (max. 30 cm H_2O), volume controlled, normo-ventilation (Servo ventilator 300, Siemens, Solna, Sweden) was obtained by using a tidal volume of 200 ml, 25 breaths/min and 8 cm H_2O in PEEP. The inspired oxygen concentration, FiO_2, was 0.21 except during periods of mCPR, when it was set to 1.0. The animals with ROSC were ventilated with a FiO_2 of 0.5. The ventilation was not synchronized with the mechanical compression–decompression cardiopulmonary resuscitation (mCPR). Ventilatory support was withdrawn during the 6.5-min periods of induced VF.

Catheters for blood pressure measurements were placed in the intrathoracic ascending aorta and the right atrium. Their position was checked at autopsy after the experiment. In three separate pigs a small incision was made just distal to the xiphoid process, and careful dissection was carried out until the pericardium could be seen. A catheter (Secalon-T over-needle central venous catheter, 16G/1.70.130 mm) was punctured into the pericardium, and the incision was closed by surgical suturing. Pressure measurements were recorded before and during VF, and compared with the right atrial pressure and the intrathoracic ascending aortic pressure. A blood flow probe was placed on the left internal carotid artery. Pressure and blood flow signals were sampled continuously by a computer during the experiment. The coronary perfusion pressure was computed as the difference between the lowest intrathoracic aortic and the lowest right atrial pressure during the decompression phase.

2.3. Mechanical chest compression-decompression

mCPR was given with LUCAS, a gas-driven device providing automatic chest compression, and active 'physiological' decompression. This is achieved by a rubber vacuum ring that brings a softened, flat, non-recoiling thorax back to its normal position during each decompression phase. Defibrillation can be safely given during on-going mCPR with this device. A detailed description of LUCAS has been given elsewhere [4].

2.4. Pilot studies

Pilot experiments were performed to decide the shortest duration of VF required to produce 100% mortality when defibrillation was the only treatment given. With the above-described protocol of anaesthesia and curarization, ventilation ($FiO_2 = 0.21$) was stopped when VF had been induced. These experiments showed that 6.5 min of VF resulted in no ROSC after three shocks given at 20-s intervals, the animals being ventilated with 100% oxygen.

2.5. Experimental protocol

Animals were randomized into three treatment groups (I–III) with 6 animals in each. The design of the experiment is shown in Fig. 1. Baseline values were registered for 30 min in all groups and did not differ between the groups. VF was induced with a 5–20 mA, 6 Hz and 30 V alternating current delivered to the epicardial surface of the heart via a needle electrode. Cardiac arrest was confirmed by abrupt decreases in arterial blood pressure and end-tidal CO_2 concentration, and an ECG showing VF, after which ventilation was stopped. After 6.5 min of VF, ventilation with 100% oxygen was started in all pigs. Defibrillation was attempted externally in all cases using a direct current (DC) shock, the first time with 200 J, second time with 300 J, and third time with 360 J. If ROSC had not occurred after 3 shocks, resuscitation was defined as unsuccessful.

In group I animals, defibrillation was attempted after 6.5 min of VF. Three shocks were given at 20-s intervals.

In group II animals, mCPR was given for 3.5 min after 6.5 min of VF. mCPR was then interrupted and the ECG and arterial blood pressure were analysed for 40 s before the first shock was given. After the shock, 10 s was allowed to judge the outcome of defibrillation. In cases of persisting VF, mCPR was re-started and continued for 30 s before a second or third shock was given, each time following 40 s periods of withdrawal of CPR. If ROSC had not been obtained after the third shock, resuscitation was defined as unsuccessful.

In group III animals, mCPR was given for 3.5 min following 6.5 min of VF. Then up to three shocks were given, if necessary, at 20-s intervals during ongoing mCPR.

2.6. Video film of the fibrillating heart

Median sternotomy was performed in three additional animals and the heart visualized by opening up the pericardium. A video camera was fixed to a support so that the heart could be filmed before induction of VF and during 6.5 min of VF. Defibrillation with 30 J was attempted after the 6.5 min by means of paddles held

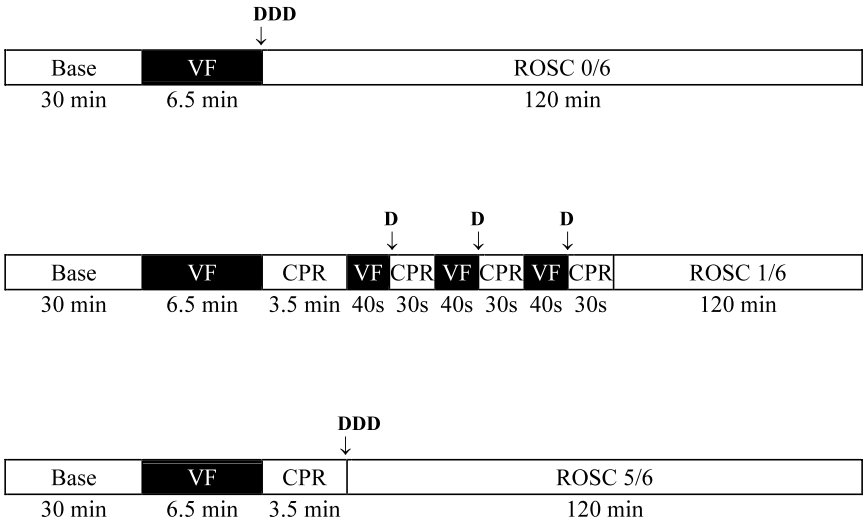

Fig. 1. The design of the experiments. The number of pigs with ROSC is indicated within the ROSC rectangle. D, defibrillation; VF, ventricular fibrillation; CPR, cardiopulmonary resuscitation.

directly against the heart. If ROSC was not obtained, internal manual heart massage was given for 3.5 min after which internal defibrillation was repeated.

2.7. Intrapericardial pressure measurement

After placement of the intrapericardial catheter and the catheters for blood pressure measurements, base line values were obtained over the next 30 min, after which ventricular fibrillation was induced.

3. Results

3.1. All groups

3.1.1. Pathophysiology during 6.5 min of VF

The intra-thoracic aortic pressure decreased rapidly to reach a minimum of 20 mmHg after about 30 s, then it increased slightly to about 25 mmHg at 2 min. Between 2 and 6.5 min it decreased gradually again to about 10 mmHg (Fig. 2). The pressure in the right atrium at first increased abruptly, then gradually to reach a peak of about 18 mmHg after 2 min. It then gradually decreased, until after 5.5 min it was equal to the intra-thoracic aortic pressure. The coronary perfusion pressure decreased from 60 to 15 mmHg within 15 s, and then gradually decreased to reach zero after about 4 min (Fig. 2). The flow in the left carotid artery also decreased quickly from 190 to about 15 ml/min after 15 s, then it gradually decreased to reach zero after about 4 min (Fig. 3). The intrapericardial pressure paralleled the right atrial pressure, but was about 2 mmHg less (Fig. 4).

3.2. Group I

3.2.1. The effect of defibrillation after 6.5 min VF

None of the animals achieved ROSC. Four animals were successfully defibrillated at the first attempt and sinus rhythm with bundle branch block was recorded. However, this was pulseless electrical activity without arterial pressure or flow.

3.2.2. The effect of 3.5 min of mCPR after 6.5 min VF

The compression pressure in the right atrium was higher than that in the intra-thoracic aorta during the first 3 min of CPR, after which the pressures equalized (Fig. 2). The decompression pressure in the intra-thoracic aorta was lower than that in the right atrium during the first minute of compressions, with the result that the coronary perfusion pressure was negative.

After about 1.5 min of mCPR the coronary perfusion pressure had reached a peak of 18 mmHg, thereafter decreasing to 12 mmHg at 3.5 min (Fig. 2). The left carotid arterial blood flow increased to 50 ml/min within 15 s (25% of the flow before VF), but decreased to about 30 ml/min after 3.5 min of compressions (Fig. 5).

3.3. Group II

3.3.1. Delayed defibrillation after 3.5 min of mCPR

Only one of six pigs achieved ROSC in this group. This animal was successfully defibrillated at the first attempt. At the end of the 2-h observation period it had a normal blood pressure. The intra-aortic compression pressure obtained is shown in Fig. 6. During the 40-s delay before defibrillation the coronary perfusion pressure fell to zero (Fig. 7). During the subsequent 30 s of mCPR the coronary perfusion pressure decreased to

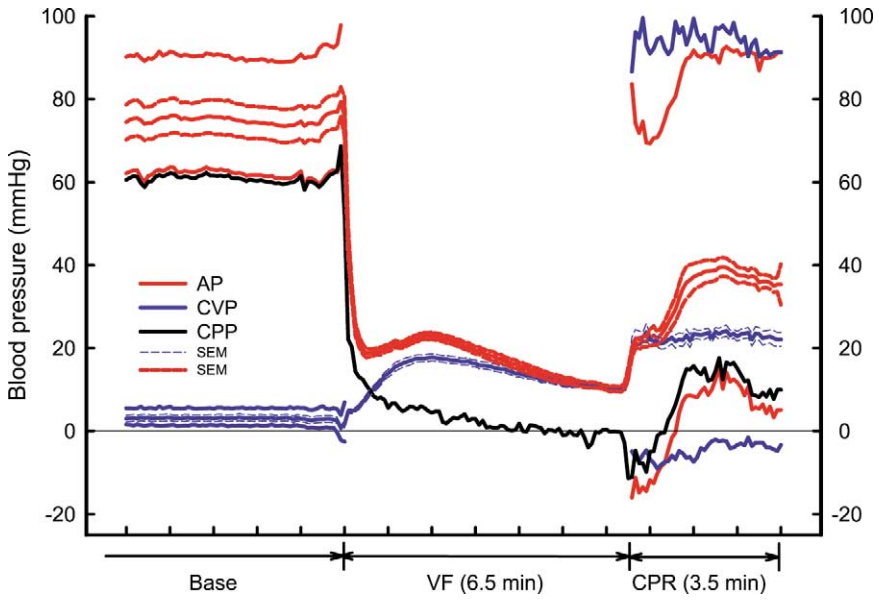

Fig. 2. Intrathoracic aortic pressure, pressure in the right atrium and computed coronary perfusion pressure are shown during 6.5 min of ventricular fibrillation followed by 3.5 min of mechanical chest compressions. Systolic, diastolic and mean pressure are shown to the left (base), and compression, decompression and mean pressure to the right (during CPR). The curves represent the mean values from 12 pigs. For the sake of clarity, the standard error of the mean is not shown in all curves.

negative values, i.e. the pressure in the right atrium was higher than that in the ascending aorta during the decompression phase. Blood flow in the left carotid artery fell to 20 ml/min after the first interruption of compressions, and had fallen to zero when the second and third defibrillation attempts were made (Fig. 5).

3.4. Group III

3.4.1. Defibrillation during on-going mCPR

Five out of six animals achieved ROSC in this group. In four of the animals ROSC was obtained after the first defibrillation attempt. In one pig, three defibrillatory shocks were given before ROSC was obtained, and in another no ROSC was obtained after three shocks. As seen in Fig. 8, the aortic systolic pressure increased by 80% to 160 mmHg 5 min after ROSC and then gradually decreased to basal values over the next 30 min. The carotid arterial blood flow curve (Fig. 9) paralleled the arterial pressure curve. After 2 h, the five animals with ROSC were stable, with pressure and blood flow that did not differ significantly from the basal values.

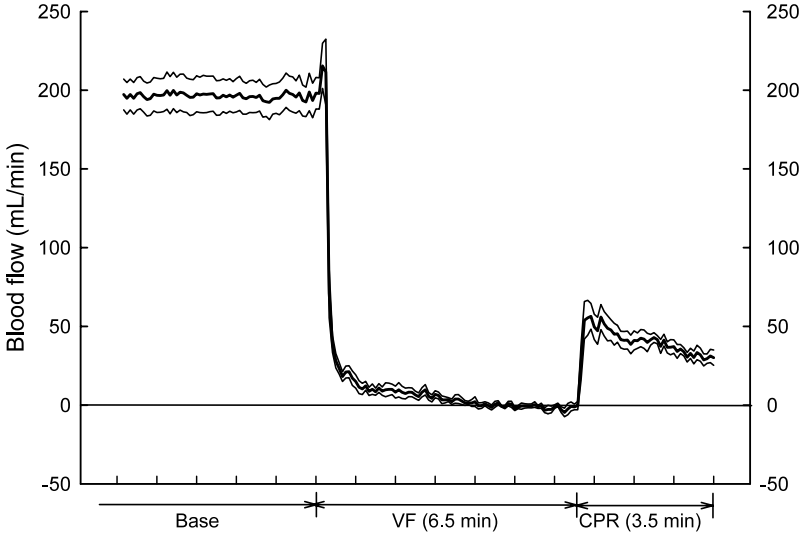

Fig. 3. The blood flow in the left internal carotide artery during 6.5 min of ventricular fibrillation followed by 3.5 min of mechanical chest compressions. The mean value±S.E.M. is shown from 12 pigs.

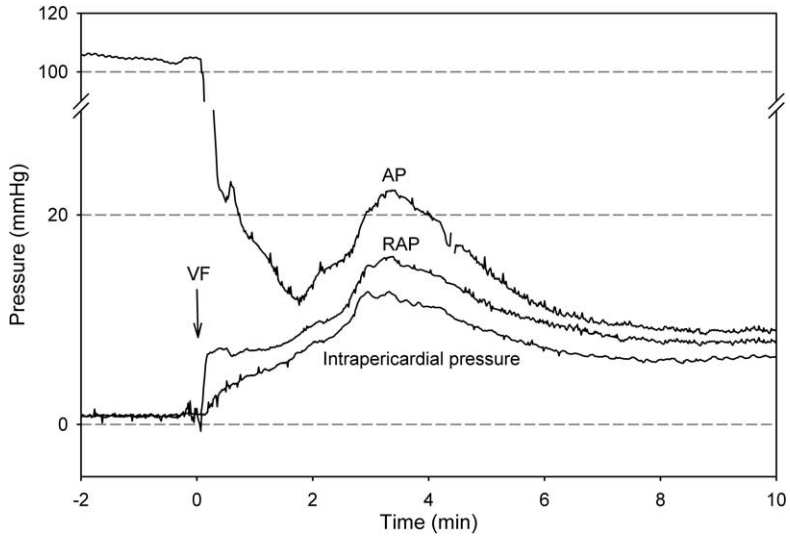

Fig. 4. Pressure recordings of the first 10 min of ventricular fibrillation in one pig in which intrapericardial pressure was also registered.

3.5. Video recording during VF

Before induction of VF, the mean heart rate of the three pigs was 110 per min, and the ECGs showed sinus rhythm. At the start of the 6.5 min VF period, the atria continued to beat with a frequency of 110 per min. By the end of the observation period, the frequency had decreased to about 60 per min. Initially the ECGs showed coarse ventricular fibrillation, but gradually the electrical activity decreased, and after 6.5 min low-voltage ventricular fibrillation was observed.

The right ventricles increased gradually in size up to 3 min, after which no further increase in size was observed by direct vision, but as judged from the light reflexes from the apex of the right ventricles their size continued to increase (Fig. 10). Dilated cardiac veins were seen on the surface of both the right and left ventricles. One attempt was made at internal defibrillation after 6.5 min and sinus rhythm, with a frequency of around 60 beats per min, was obtained in two of the three animals. No increase in blood pressure was observed; the greatly distended right ventricles did not move. The less-than-normal sized left ventricles were seen to contract at the same frequency as the atria, but without creating pressure in the intra-thoracic aorta. After about 20 s, ventricular fibrillation recurred in the two animals with sinus rhythm. Internal manual heart compressions were then given for 3.5 min after which the right ventricles had regained a normal size, and coarse VF could be seen on the ECG in all three animals. One shock was given

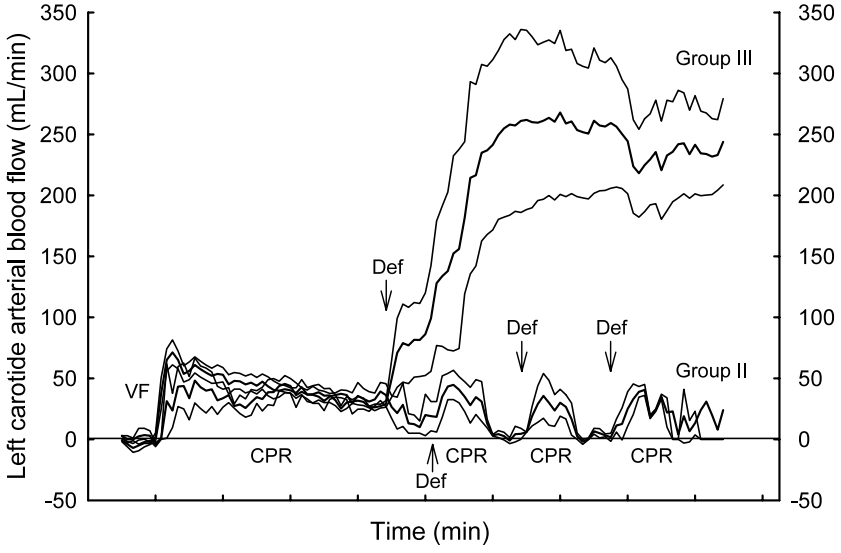

Fig. 5. The blood flow in the left internal carotide artery during 3.5 min of mechanical compressions followed by defibrillation attempts with (II) and without (III) interrupting the chest compressions. Mean value ± S.E.M., $n = 5$ in each group (the one pig which survived in group II and the one pig which died in group III are excluded to get a clear non-ROSC vs. ROSC group).

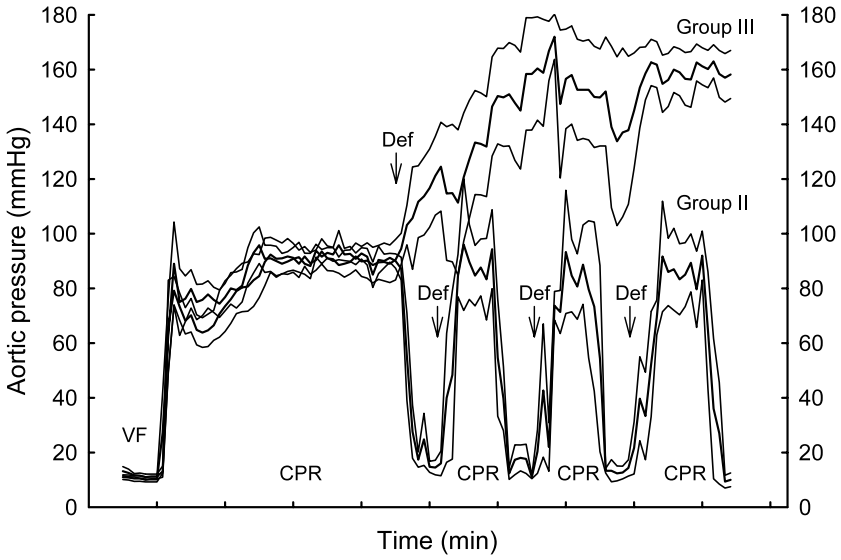

Fig. 6. Intrathoracic aortic compression pressure during 3.5 min of mechanical compressions followed by defibrillation with (II) and without (III) interrupting the chest compressions. Mean value ± S.E.M., $n = 5$ in each group.

directly to the heart while continuing massage with the metallic defibrillation paddles. ROSC was obtained in all three animals.

3.5.1. Intrapericardial pressure recording during VF

In all three pigs, the intrapericardial pressure followed the pressure in the right atrium, but was 1–2 mmHg less. Recordings from one of these experiments are shown in Fig. 4.

4. Discussion

It has been estimated that 375 000 people in Europe [5] and 275 000 in the USA [6] are victims of sudden cardiac arrest each year. The great majority of these cases occur out of hospital. For the last 40 years the 1-year survival rate has remained extremely poor (less than 5%) despite efforts to improve emergency care and the increasing availability of automated external defibrillators (AEDs). About half of all deaths in the Western world are caused by cardiovascular disease, and about half of all cardiovascular deaths are due to out-of-hospital cardiac arrest [6]. These continuing poor results warrant a radical new approach to the treatment of this most common and most dramatic of all diseases.

Cardiac arrest is manifest either as VF or, in an appreciable minority of cases, as pulseless electrical activity (PEA) or asystole. Defibrillation will obviously not save a patient with asystole but has a good chance of

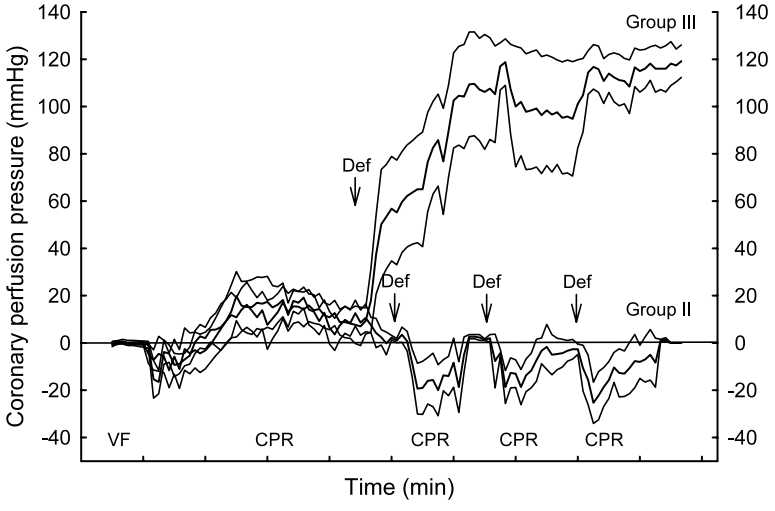

Fig. 7. Coronary perfusion pressure during 3.5 min of mechanical compressions and during defibrillation attempts with (II) and without (III) interrupting the chest compressions. Mean value ± S.E.M., $n = 5$ in each group.

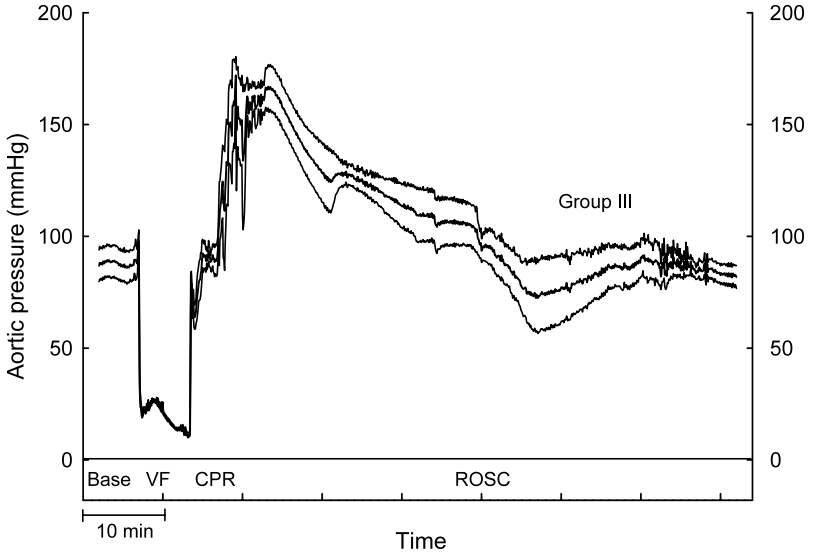

Fig. 8. Systolic intrathoracic aortic pressure during the first hour after ROSC. Mean value ± S.E.M., $n = 5$.

success in VF if a shock can be given within 4–5 min of its onset. Only a tiny minority of cardiac arrest victims can be defibrillated within that short period of time.

The present study sheds light on the pathophysiology of acute ventricular fibrillation. Blood is pooled in the venous circulation, with the result that the right heart becomes more and more distended and the left heart more and more empty over about 3 min of VF. When the blood pressure on the arterial side equals that on the venous side, after about 5 min, the coronary perfusion pressure and the carotid flow fall to zero. When chest compressions are initiated, flow in the carotid artery increases to acceptable values within 10 s, but it takes 1 min to bring a negative coronary perfusion pressure back to zero, and a further half minute to bring it up to an adequate level. This time discrepancy is due to the different effects of chest compression on the haemodynamics within and outside the thorax. Extrathoracic organs (e.g. the brain) receive perfusion pressure and flow during both the compression and decompression phases. The arrested heart, however, is only perfused during the decompression phase, since the pressure in the ascending aorta is less or equal to the pressure in the right atrium during the compression phase (Fig. 2). Furthermore, as the right heart becomes more and more distended, the coronary pressure needed to provide adequate perfusion increases correspondingly.

In the group I animals, sinus rhythm was achieved by defibrillation after 6.5 min of VF, but there was no detectable arterial pressure or flow (PEA). At this time the right ventricle remained greatly distended and did not move, while the empty and non-stretched left

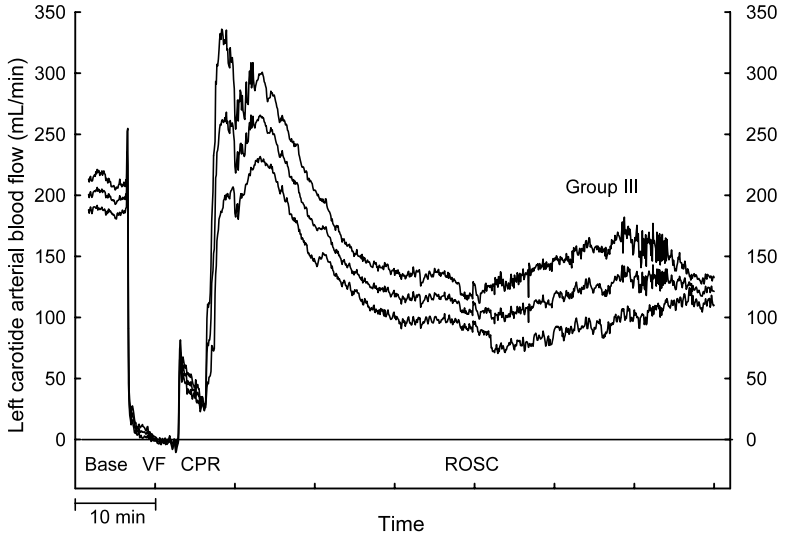

Fig. 9. The blood flow in the left internal carotide artery during the first hour after ROSC. Mean value ± S.E.M., $n = 5$.

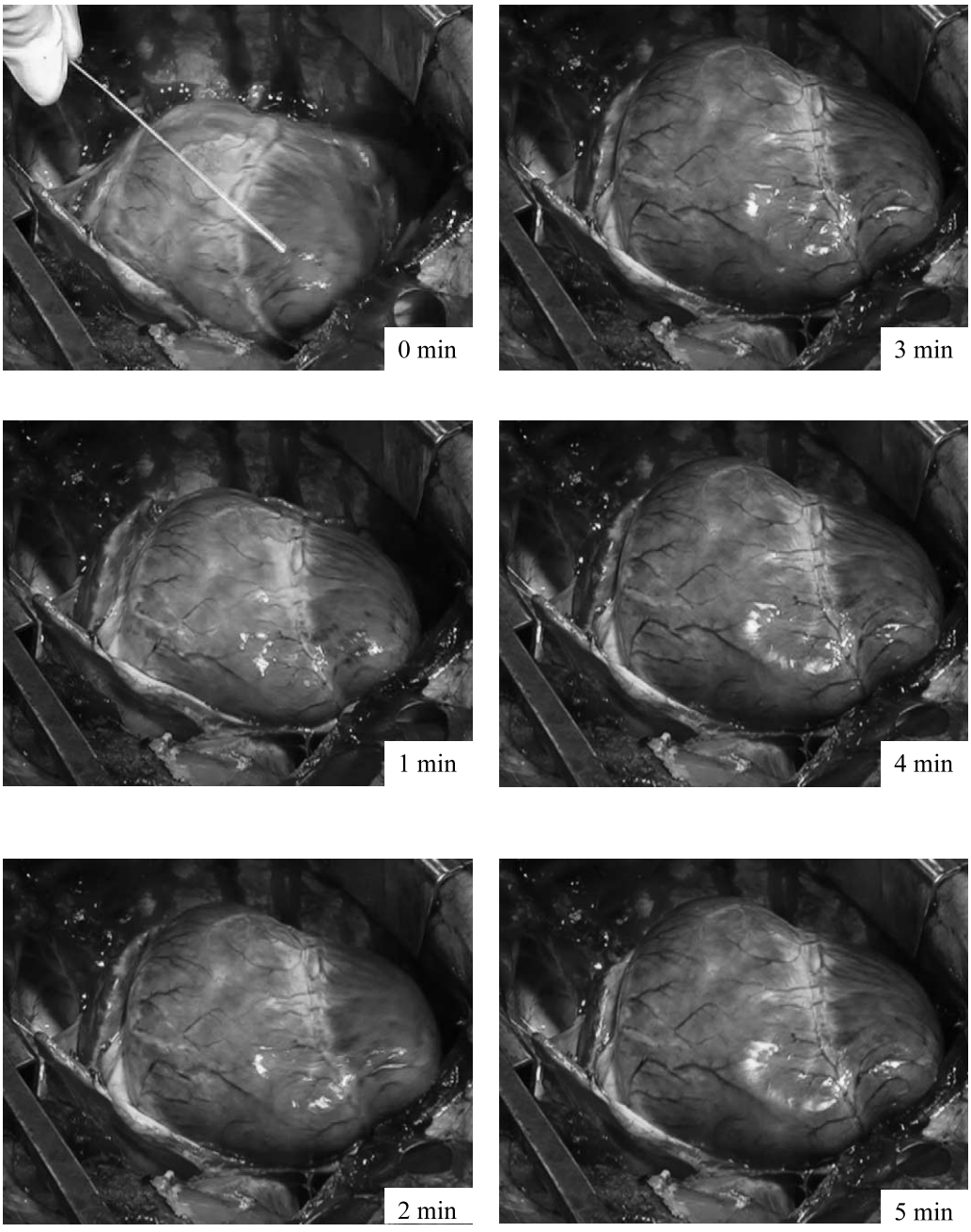

Fig. 10. Frozen pictures from the video uptake after induction of ventricular fibrillation.

ventricle was seen to contract without coronary perfusion pressure. It seems important, therefore, in the treatment of prolonged VF, to give chest compressions before attempting defibrillation, otherwise the physiological requisites for ROSC are absent.

In the absence of immediate restoration of an effective heart beat there is another reason why immediate chest compressions are vitally important for full functional recovery. By the time rescue efforts are under way, the brain has already been subjected to minutes of hypoxia and some flow must be restored as quickly as possible. The initial period of compressions serves two purposes: preservation of brain function during a period of continuing vulnerability, and priming of the heart for successful restoration of the heart beat.

As seen in Fig. 2, one min of compressions (i.e. 100 adequate compressions) was needed to bring the coronary perfusion pressure back to zero, and a further 30 s (50 compressions) to produce a coronary perfusion pressure of 15 mmHg, i.e. the minimum pressure needed for a predictable ROSC [4,7]. Wik et al. recently presented the results from a randomized clinical study

of witnessed out-of-hospital cardiac arrest in about 200 patients [2]. In cases in which CPR was not initiated until 5 min or more after the onset of VF, 3 min of external manual chest compressions before the first defibrillation attempt increased the 1-year survival rate to 20%. This compared with 4% survival in the group treated according to current guidelines with defibrillation as the first-step strategy. Thus, the suggestions of Cobb et al. [1] and Wik et al. [2], to perform chest compressions for 1.5 or 3 min before the first defibrillation attempt, is supported by the findings of the present study.

Interrupting chest compressions reduces the chance of successful ROSC due to the immediate loss of an adequate coronary perfusion pressure. As can be seen in Fig. 7, 30 s of compressions (= 50 compressions) between defibrillation attempts were not enough to create a positive coronary perfusion pressure, although the carotid flow increased to acceptable values (Fig. 5). Even the interruption of chest compressions for rescue breathing during CPR has been reported to give adverse haemodynamic effects [8,9]. It seems, therefore, that defibrillation should be attempted during and not after a period of chest compression. This would clearly not be feasible, or safe, during manual chest compression. It would be possible to reduce to a minimum the interval between stopping compressions and applying a manual defibrillator. On the other hand, automated external defibrillators (AEDs) currently require a significant 'hands off' period whilst analysis of the ECG rhythm takes place. Using mechanical chest compression (mCPR) is one way in which defibrillation can be safely and efficiently carried out during on-going chest compression.

To conclude, a fibrillating, distended heart should be treated by continuous chest compressions for at least for 90 s prior to defibrillation which should, ideally, be carried out during on-going compressions.

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