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Oxygen delivery and return of spontaneous circulation with ventilation:compression ratio 2:30 versus chest compressions only CPR in pigs

E. Dorph [a,b,d,*], L. Wik [c,d], T.A. Strømme [b], M. Eriksen [b], P.A. Steen [d]

[a] *Norwegian Air Ambulance, N-1441 Drøbak, Norway*
[b] *Institute for Experimental Medical Research, Ullevål University Hospital, N-0407 Oslo, Norway*
[c] *National Centre of Competence for Emergency Medicine, Ullevål University Hospital, N-0407 Oslo, Norway*
[d] *Division of Emergency Medical Services, Ullevål University Hospital, N-0407 Oslo, Norway*

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Abstract

The need for rescue breathing during the initial management of sudden cardiac arrest is currently being debated and reevaluated. The present study was designed to compare cerebral oxygen delivery during basic life support (BLS) by chest compressions only with chest compressions plus ventilation in pigs with an obstructed airway mimicked by a valve hindering passive inhalation. Resuscitability was then studied during the subsequent advanced life support (ALS) period. After 3 min of untreated ventricular fibrillation (VF) BLS was started. The animals were randomised into two groups. One group received chest compressions only. The other group received ventilations and chest compressions with a ratio of 2:30. A gas mixture of 17% oxygen and 4% carbon dioxide was used for ventilation during BLS. After 10 min of BLS, ALS was provided. All six pigs ventilated during BLS attained a return of spontaneous circulation (ROSC) within the first 2 min of advanced cardiopulmonary resuscitation (CPR) compared with only one of six compressions-only pigs. While all except one compressions-only animal achieved ROSC before the experiment was terminated, the median time to ROSC was shorter in the ventilated group. With a ventilation:compression ratio of 2:30 the arterial oxygen content stayed at 2/3 of normal, but with compressions-only, the arterial blood was virtually desaturated with no arterio-venous oxygen difference within 1.5–2 min. Haemodynamic data did not differ between the groups. In this model of very ideal BLS, ventilation improved arterial oxygenation and the median time to ROSC was shorter. We believe that in cardiac arrest with an obstructed airway, pulmonary ventilation should still be strongly recommended.
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Keywords: CPR; Mouth-to-mouth; Ratios; Oxygen delivery; Return of spontaneous circulation

Resumo

A necessidade de insuflações de emergência durante a fase inicial da abordagem da paragem cardíaca súbita está actualmente em debate e a ser reavaliada. Este estudo foi desenhado para comparar o fornecimento cerebral de oxigénio durante o suporte básico de vida (BLS) só com compressões torácicas e com compressões torácicas e insuflações, em porcos com a via aérea obstruída através de uma válvula. A reanimabilidade era depois estudada no período subsequente de suporte avançado de vida (ALS). Após 3 minutos de fibrilhação ventricular iniciava-se BLS. Os animais eram distribuídos aleatoriamente em dois grupos. Um, recebia apenas compressões torácicas. O outro recebia ventilações e compressões à razão de 2:30. Usou-se uma mistura gasosa de 17% de oxigénio e 4% de dióxido de carbono para a ventilação durante o BLS. Ao fim de 10 min de BLS, iniciava-se o ALS. Os seis porcos ventilados durante o BLS atingiram um retorno de circulação espontânea (ROSC) nos primeiros 2 min de reanimação cardio-pulmonar avançada quando comparados com apenas um dos porcos dos que só receberam compressões. Só um dos animais do grupo apenas com compressões não conseguiu ROSC antes de terminar a experiência. O tempo médio até atingir ROSC era menor no grupo ventilado. Quando a razão ventilação: compressão era de 2:30 a concentração arterial de oxigénio permaneceu em 2/3 do normal, mas no grupo só com compressões, o sangue arterial estava virtualmente dessaturado, sem diferença artério-venosa de oxigénio ao fim de 1.5–2 min. Os dados hemodinâmicos não diferiram entre os grupos. Neste modelo de BLS

* Correponding author. Tel.: +47-23016813; fax: +47-23016799.
E-mail address: Elizabeth@nakos.org (E. Dorph).

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ideal, a ventilação melhorou a oxigenação e o tempo médio para ROSC foi mais curto. Acreditamos que, na paragem cardíaca com via aérea obstruída, a ventilação pulmonar deve continuar a ser fortemente recomendada.
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Palavras chave: CPR; Boca-a-boca; Razões; Fornecimento de Oxigénio; Regresso de circulação espontânea

Resumen

La necesidad de ventilaciones de rescate durante el manejo inicial de paro cardíaco súbito está actualmente siendo debatido y reevaluado. El presente estudio fue diseñado para comparar la entrega de oxigeno cerebral durante el soporte vital básico (BLS) con aplicación solamente de compresiones o con compresiones y ventilaciones en cerdos con una vía aérea obstruida simulada con una válvula que evita la inhalación pasiva. La resucitabilidad fue entonces estudiada durante el período de soporte vital avanzado (ALS) subsecuente. Después de tres minutos de fibrilación ventricular(VF) sin tratamiento se inició BLS. Los animales fueron randomizados en dos grupos. Un grupo recibió solo compresiones torácicas. El otro grupo recibió ventilaciones y compresiones torácicas en una relación 2:30. Se uso una mezcla de gas con 17% de oxígeno y 4% de dióxido de carbono durante el BLS. Después de 10 minutos en BLS, se proporcionó ALS. Los 6 cerdos ventilados durante el BLS alcanzaron retorno a circulación espontánea(ROSC) dentro de los primeros 2 minutos de reanimación cardiopulmonar (CPR) avanzada comparados con solo uno de seis de los cerdos manejados solo con compresiones. Mientras todos salvo un animal del grupo solo compresiones alcanzó ROSC antes de terminar el experimento, la mediana de tiempo a ROSC fue mas corta en el grupo ventilado. Con una relación ventilación : compresión de 2:30 el contenido arterial de oxígeno se mantuvo en 2/3 de lo normal, pero solo con compresiones el contenido arterial de oxígeno fue virtualmente desaturado, sin diferencia arteriovenosa de contenido de oxígeno, al cabo de 1.5–2 minutos. Los datos hemodinámicos no difirieron entre los grupos. En este modelo de BLS muy ideal, la ventilación mejoró la oxigenación arterial y la media de tiempo a ROSC fue mas corta. Creemos que en el paro cardíaco con vía aérea obstruida, la ventilación está fuertemente recomendada.
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Palabras clave: RCP; Boca a boca; Relación; Entrega de oxígeno; Retorno a circulación espontánea

1. Introduction

Bystander cardiopulmonary resuscitation (CPR) improves the chances of successful resuscitation and survival [1,2]. The presently recommended procedure for lay rescuer CPR includes a combination of two rescue breaths interposed after every 15th chest compression [3]. Over the past decade, the need for assisted ventilation in treatment of adult patients with primary cardiac arrest has been challenged and re-evaluated [4–7]. One reason for this re-evaluation is the fact that both lay rescuers and professional medical providers are reluctant to perform mouth-to-mouth ventilation owing to concerns about transmission of infectious diseases [8–10]. In addition, the current basic CPR technique is a complex psychomotor task that is difficult to learn and perform without complications such as gastric inflation [11–13]. Finally, the relatively long pauses in chest compression required for ventilation interrupt the CPR-generated perfusion, potentially compromising the success of cardiac resuscitation [14–16].

On this basis, some investigators have begun to explore ventilation:compression ratios with much longer sequences of uninterrupted compressions [14,17] or even chest compressions only CPR [7,18–20].

Based on theoretical considerations Babbs and Kern [21] recently suggested that a ratio of 2:30 would be ideal during basic life support (BLS) with pauses in chest compressions of 2.5 s per breath, and in a previous study of different ventilation:compression ratios we found oxygen saturation data supporting that a ratio near 2:30 might be optimal for standard, guidelines specified, BLS [22].

The purpose of the present study was to compare BLS by compressions-only to a ventilation-compression ratio of 2:30 for 10 min followed by standard advanced life support (ALS) in a pig model of ventricular fibrillation (VF). The primary outcome variables were the calculated carotid and cerebrocortical oxygen delivery during BLS and time to return of spontaneous circulation in the ALS period.

It was our hypothesis that adequate oxygen delivery and favourable resuscitation outcome may be maintained with ventilation:compression ratio of 2:30 whilst compressions-only CPR would result in rapid arterial deoxygenation and compromised resuscitability.

2. Materials and methods

2.1. Animal preparation

The experiments were conducted in accordance with “Regulations on Animal Experimentation” under The Norwegian Animal Welfare Act and approved by Norwegian Animal Research Authority. Thirteen healthy domestic swine of either sex and 10–12 weeks of age were fasted over night but were given free access to water. The animals were sedated with a single intramuscular injection of ketamine (30 mg kg^{-1}) and atropine 1 mg and then placed supine in a U-shaped cradle with a heating blanket inter-

posed between the back and the cradle and the limbs secured to prevent body displacement during the performance of CPR. After ear vein catheter insertion bolus injections of sodium pentobarbital (15–25 mg kg^{-1}) and fentanyl 100 μg were given. Anaesthesia was maintained with continuous infusions of sodium pentobarbital (5–10 mg kg^{-1} $h^{-1)}$ and fentanyl (30–50 μg kg^{-1} h^{-1}). During preparation acetated Ringer's solution (25 ml kg^{-1} h^{-1}) was administered. The animals received a tracheotomy and were mechanically ventilated (Servo Ventilator 900 B, Siemens-Elema AB, Solna, Sweden) with ambient air.

The ventilation was volume was controlled with a fixed frequency of 16 breaths min^{-1}, positive end-expiratory pressure of 2–3 cm H_2O and the tidal volume adjusted to maintain an end-tidal carbon dioxide ($ETCO_2$) level of 4.5–5.5 kPa as measured by the gas monitor (Datex Capnomac Ultima™, Helsinki, Finland). Urine was drained continuously through a cystostoma, and the intra-abdominal temperature was maintained at 38.5–39.5 °C throughout the experimental period.

A 7F micro-tip pressure transducer catheter (Model SPC 470, Millar Instruments, Houston, TX, USA) was inserted through the right femoral artery and advanced to the descending aorta at the level of the heart for continuous arterial pressure monitoring. Another 7F micro-tip pressure transducer catheter (Millar Instruments) was introduced into the left ventricle through the left common carotid artery to measure the left ventricular pressure. A 7F Swan-Ganz® catheter (model 131HF7, Baxter Healthcare Corporation, Irvine, CA, USA) was advanced through the right femoral vein and flow directed into the right atrium for pressure recordings and mixed venous blood sampling. A 7.5F Swan-Ganz® CCOmbo catheter (model 744HF75, Edwards Lifesciences LLC, Irvine, Ca, USA) was inserted into the descending aorta via the left femoral artery for continuous arterial oxygen saturation monitoring and sampling of arterial blood. After ligation of all visible extracranial branches of the right common carotid artery a transit-time ultrasound flowmetry probe (model 3SB880, Transonic Systems Inc, Ithaca, NY, USA) was applied to the right internal carotid artery. All invasive catheters were introduced using a cut-down technique.

To monitor cerebral cortical blood flow the technique of laser-Doppler flowmetry (LDF) was applied. This method allows continuous measurement of focal microcirculatory blood flow and the LDF readings are expressed in arbitrary perfusion units (PU) [23,24].

The right parietal region of the skull was exposed. A burr hole of 12–15 mm in diameter was drilled in the cranium using an electric drill (Dremel® Minicraft, Germany) at low speed. A gentle saline drip (0.9%, 25 °C) over the drilling site prevented thermal injury to the cortex. and adjacent tissues. The centre of the hole was located 12–15 mm lateral to the sagittal suture and 12–15 mm anterior to the coronal suture. The dura was opened and a laser-Doppler probe (model 407. Perimed AB, Stockholm, Sweden), connected to a perfusion monitor (PeriFlux System 5000, Perimed AB, Stockholm, Sweden), with probe holder (model PH 07-4, Perimed AB, Stockholm, Sweden) was secured on the surface of the cortex in a position carefully chosen to avoid visible pial vessels. The burr hole was then sealed with bone wax.

The Swan-Ganz catheter in the right atrium and the side port lumen of the micro-tip transducer catheter in the descending aorta were connected to fluid filled transducers (Statham® P23Dd, Gould Instruments, Hato Rey, Puerto Rico).

Tidal volumes, respiratory pattern and $ETCO_2$ were measured continuously using a combined differential pressure pneumotach flow sensor and solid state CO_2 sensor in combination with a respiratory profile monitor (CO_2SMO Plus! Model 8100, Novametrix Medical System Inc., Wallingford, CT, USA). The flow/CO_2 sensor was inserted in the breathing circuit between the ventilator and a bacterial filter connected to the tracheal tube. The monitor was connected on-line to a computer (Omnibook 6000, Hewlett Packard Company, Cupertino, Ca, USA) into which the data were downloaded, stored and analysed using Analysis Plus! version 3.0 Software package (Novametrix Medical System Inc.).

Pressures, carotid flow signals and laser-Doppler flow signals were sampled using PC-based real time data acquisition hardware (DaqBoards™ Model 200A, IOtech Inc., Cleveland, OH, USA) supported with software for DASYLab version 5.1 (Datalog, National Instruments company, Moenchengladbach, Germany) and printed on an eight-channel thermal array recorder model TA 11 (Gould Instrument Systems Inc., Ohio, USA). Arterial oxygen saturation was continuously recorded using the Swan-Ganz® CCOmbo catheter connected to an oximetry monitor (Vigilance®, Edwards Critical-Care Division, Irvine, Ca, USA). Arterial blood gas specimens were obtained from the thoracic aorta and mixed venous specimens were obtained from the right atrium at baseline (before cardiac arrest) and during CPR. Oxygen saturation, haemoglobin levels (OSM3Hemoximeter®, Radiometer, Copenhagen, Denmark) and blood gases (AVL OMNI™ 9, AVL List GmbH Medizintechnik, Graz, Austria) were measured.

Standard lead II of the surface ECG was monitored (Lifepak® 12 3D Biphasic, Medtronic Physio-Control, WA, USA) throughout the experimental protocol using separate ECG recording electrodes (Conmed®, NY, USA). Self-adhesive defibrillation electrodes (Quik-Combo™, Physio-Control Corporation, WA, USA) were applied to the shaved thorax. One electrode was placed at or near the cardiac apex, and the second electrode was placed on the right chest wall in a somewhat higher thoracic position.

2.2. Machinery

Consistent optimal chest compressions were achieved by use of a modified automatic hydraulic battery driven chest compression device (Heartsaver 2000®, Medreco, Bodø,

Norway) with equal compression-relaxation phases. The piston movement was photoelectrically controlled; compression depth was set at 4 cm with a frequency of 100 per minute.

2.3. Experimental protocol

After collecting all necessary baseline (pre-VF) data, pancuronium bromide (Pavulon®, N.V. Organon, Oss, The Netherlands) 0.25 mg kg^{-1} was administered to prevent spontaneous ventilation during cardiac arrest. Intravenous infusions and ventilation were stopped immediately before induction of ventricular fibrillation, which was induced by an alternating current applied trans-thoracically for 3 s. Fibrillation was indicated by an abrupt fall in aortic pressure and confirmed by the ECG tracing. A 3 min interval of untreated VF was followed by a 10 min BLS period. Animals were randomly assigned to receive 10 min of chest compressions plus ventilation or 10 min of chest compressions without ventilatory support. Chest compressions were delivered mechanically at a rate of 100 min^{-1}.

Ventilation, when provided, was administered with an adult-sized manual bag (Laerdal, Stavanger, Norway) using a gas mixture of 17% oxygen and 4% carbon dioxide, consistent with expired air from a rescue breather [25]. Chest compression cycles were interrupted for delivery of the ventilatory breaths. A ventilation/compression ratio of 2:30 was used and each inhalation was applied over 1.0–1.5 s. An impedance threshold valve (ITV Resusci-Valve, CPR$_x$LLC, Minneapolis, USA) in impedance mode was connected to the external end of the tracheal tube throughout the BLS period to hinder passive inspiratory airflow secondary to chest recoil during the decompression phase. This valve does not impede the expiratory air flow, but in the impedance mode it prevents inspiratory flow for negative intrathoracic pressures less than 36–37 cm H_2O [26].

After the BLS period (13 min after VF induction), all animals received ALS according to the international guidelines [27]. Animals received as many as three consecutive defibrillation attempts starting with 100 J on the first two biphasic shocks, followed by 150 J on subsequent attempts. If the animals failed to achieve a return of spontaneous circulation (ROSC) after these initial attempts at defibrillation, continuous chest compressions were initiated and without interruption manual ventilation was interposed once every 8th compression (12.5 ventilations per min) [28] using 100% oxygen. Adrenaline (epinephrine) 0.02 mg kg^{-1} was administered intravenously and further attempts to defibrillate were donemade as recommended in the guidelines [27]. If spontaneous circulation was not restored within 10 min of ALS, resuscitative efforts were discontinued. ROSC was defined as an unassisted pulsatile rhythm with a systolic aortic pressure greater than 60 mmHg maintained for at least 1 min.

Carotid flow, cerebral cortical blood flow, all pressures, respiratory variables, $ETCO_2$ and arterial oxygen saturation were recorded continuously throughout the experimental period. Arterial and mixed venous blood gases were sampled 4, 6, 9 and 12 min post-VF.

Whether ROSC was achieved or not, the time to ROSC, the total number of defibrillation attempts, and number of doses of adrenaline were registered.

At the end of the experiment surviving animals were killed with intravenous pentobarbital. An autopsy was performed on all pigs to check for damage to the rib cage and internal organs and for verification of catheter placements.

2.4. Calculations

All haemodynamic pressures, focal cerebral cortical microcirculation and carotid flow were analysed by exporting the raw data into a specially constructed program designed in a mathematics software package (MATLAB®, The MathWorks Inc., Natick, MA, USA).

The chest compression rate during CPR was set at 100 min^{-1}. The sampling frequency for the pressure and flow signals were 200 Hz, hence there were 120 sampling points for each compression:decompression cycle. As the duty cycle was 50:50, the decompression phase was defined as the period ±30 sampling points from the middle point between two peak compressions. Early, mid and late decompressions were then defined as being the first, mid and last 20 sampling points of this period. Mean decompression represents the mean of all sampling points in the decompression phase.

Coronary perfusion pressure (CPP) was calculated as the difference between thoracic aortic and right atrial pressures in the decompression phase using an electronic subtraction unit.

Cerebral cortical blood flow (CCBF) levels during chest compressions were calculated as a fraction of baseline flow. Measured baseline PU values for CCBF were considered 100% and changes were given as a percentage (%) of these values.

Carotid oxygen delivery (ml min^{-1}) was computed by multiplying arterial oxygen content (CAO_2) times the carotid blood flow (dl min^{-1}). The product % of % PU min^{-1} times Cao_2CaO_2 was calculated as an estimate of cerebrocortical oxygen supply.

2.5. Statistical analysis

The data were analyzed using the statistical software package SPSS (SPSS Inc., Chicago, IL, USA). Based on evaluation of the data distribution they are presented as mean±S.D. or median (25, 75 percentile). Categorical variables were analyzed with Fisher's exact test. The overall haemodynamic, blood gas, and oxygen delivery data were summarized using the area under the curve (AUC) technique [29]. Unpaired Student's *t* test was used to analyze differences in AUC between the groups, and between group differences at some time points. Numerical outcome data were evaluated with two-tailed Wilcoxon rank sum test.

Table 1
Measured and calculated pressures (mmHg) at baseline and during CPR

	Baseline	During CPR			
		1 min	3 min	6 min	9 min
Compressions-only					
Aortic pressure					
Mean	92 ± 17	37 ± 5	41 ± 8	35 ± 10	33 ± 10
Peak compression		85 ± 18	92 ± 12	88 ± 14	88 ± 20
Mean decompression		23 ± 4	26 ± 9	18 ± 10	15 ± 9
Right atrial pressure					
Mean	9 ± 4	55 ± 22	53 ± 19	46 ± 11	44 ± 12
Peak compression		175 ± 83	151 ± 67	146 ± 48	146 ± 52
Mean decompression		15 ± 10	15 ± 8	11 ± 5	10 ± 5
Left ventricular pressure					
Mean	53 ± 12	49 ± 17	48 ± 14	40 ± 8	38 ± 10
Peak compression		160 ± 63	152 ± 53	139 ± 37	132 ± 38
Mean decompression		10 ± 6	11 ± 6	7 ± 5	7 ± 4
Coronary perfusion pressure					
Mean decompression		15 ± 2	16 ± 4	12 ± 6	11 ± 7
Ratio 2:30					
Aortic pressure					
Mean	90 ± 24	41 ± 12	46 ± 13	40 ± 10	37 ± 8
Peak compression		95 ± 34	111 ± 57	97 ± 30	90 ± 29
Mean decompression		27 ± 9	30 ± 7	25 ± 7	26 ± 6
Right atrial pressure					
Mean	9 ± 2	50 ± 13	50 ± 21	44 ± 15	42 ± 13
Peak compression		143 ± 48	135 ± 80	119 ± 63	107 ± 57
Mean decompression		15 ± 5	16 ± 5	15 ± 5	16 ± 6
Left ventricular pressure					
Mean	53 ± 12	52 ± 11	58 ± 15	48 ± 6	46 ± 6
Peak compression		174 ± 31	192 ± 45	159 ± 15	151 ± 19
Mean decompression		10 ± 4	11 ± 5	10 ± 3	9 ± 3
Coronary perfusion pressure					
Mean decompression		17 ± 7	16 ± 4	16 ± 5	14 ± 5

There were no significant differences between the groups.

3. Results

Ventricular fibrillation was obtained in 13 pigs (weight 27 ± 4 kg) by the first trans-thoracic shock. One pig was excluded from analysis due to inadequate pressure and flow recordings. In the remaining 12 pigs no gross liver, lung, heart or other visceral damage was found at autopsy.

The inspiratory impedance valve connected to the external end of the tracheal tube was successful in completely inhibiting chest decompression-induced inflation. With the first 15–20 chest compressions there was some expiratory air flow.

There were no significant differences between the two groups in baseline data before induction of VF (Tables 1–3). After 3 min of untreated VF arterial oxygen saturation was not significantly lower than baseline (Fig. 1).

3.1. Blood flows

Mean carotid blood flow remained above 25% and mean cerebral cortical blood flow above 20% of pre-arrest baseline throughout the basic CPR period with no significant difference between methods (Table 2).

3.2. Measured and calculated pressures

No significant differences in any pressures were found at any time during the study (Table 1).

3.3. Blood gases, arterial oxygen saturation and ventilation

After 1 min of BLS the arterial pO_2, oxygen saturation (Table 3) and pH were significantly higher and the arterial pCO_2 significantly lower in the ventilated group. Mixed venous blood gases showed expected changes from baseline with rising pCO_2 levels and declining pH, BE, pO_2 and oxygen saturation. After 6 min of BLS mixed venous pCO_2 and pO_2 were significantly different between the two groups. For the non-ventilated group there was no arterio-venous difference in pO_2 after 3 min of CPR.

Table 2
Internal carotid artery blood flow, cerebral cortical blood flow (CCBF) and calculated oxygen delivery at baseline and during CPR

	Baseline	During CPR				*P*
		1 min	3 min	6 min	9 min	
Average flow per minute						
Compressions-only						
Carotid flow (ml)	145 ± 20	56 ± 12	52 ± 12	39 ± 8	36 ± 9	0.542
CCBF (% of baseline PU)	100	46 ± 21	42 ± 23	31 ± 21	27 ± 19	0.109
Ratio 2:30						
Carotid flow (ml)	130 ± 40	49 ± 24	40 ± 20	38 ± 16	34 ± 11	
CCBF (% of baseline PU)	100	28 ± 11	24 ± 7	22 ± 6	21 ± 6	
Oxygen delivery per minute						
Compressions-only						
Carotid (ml)	16.3 ± 3.6	1.7 ± 0.8	0.4 ± 0.3	0.2 ± 0.1	0.2 ± 0.1	<0.001
Cortical (% PU·Cao$_2$)	1101 ± 100	144 ± 130	29 ± 36	14 ± 10	12 ± 5	<0.001
Ratio 2:30						
Carotid (ml)	15.0 ± 5.1	3.8 ± 1.5	3.1 ± 1.5	3.1 ± 1.5	2.7 ± 1.0	
Cortical (% PU·CaO$_2$)	1129 ± 41	222 ± 113	189 ± 50	175 ± 38	156 ± 41	

P values vs. ratio 2:30 using area under curve analysis.

Table 3
End-tidal CO_2 ($ETCO_2$), arterial oxygen content (ml dl$^{-1)}$), arterial and mixed venous blood gases at baseline and during CPR

	Baseline	During CPR				*P*
		1 min	3 min	6 min	9 min	
Compressions-only						
$ETCO_2$ (kPa)	5.0 ± 0.3	0	0	0	0	
Arterial blood gas						
pH	7.45 ± 0.04	7.26 ± 0.05	7.19 ± 0.04	7.12 ± 0.06	7.05 ± 0.07	<0.01
pCO_2 (kPa)	5.2 ± 0.5	8.7 ± 0.8	10.2 ± 0.9	11.6 ± 1.1	13.0 ± 1.5	<0.01
pO_2 (kPa)	11.9 ± 1.8	3.3 ± 1.4	2.1 ± 0.6	2.0 ± 0.7	2.1 ± 0.4	<0.001
BE	2.4 ± 1.0	−0.0 ± 1.9	−1.9 ± 1.7	−4.2 ± 2.3	−6.7 ± 2.9	0.929
O_2 saturation (%)	96 ± 3	23 ± 11	6 ± 4	4 ± 2	4 ± 1	<0.001
Oxygen content (ml dl^{-1})	11.0 ± 1.0	2.6 ± 1.2	0.7 ± 0.5	0.5 ± 0.3	0.5 ± 0.1	<0.001
Venous blood gas						
pH	7.40 ± 0.03	7.23 ± 0.05	7.18 ± 0.05	7.10 ± 0.06	7.03 ± 0.08	0.153
pCO_2 (kPa)	5.9 ± 0.6	9.2 ± 0.7	10.4 ± 0.9	11.8 ± 1.3	13.4 ± 1.8	<0.05
pO_2 (kPa)	6.2 ± 0.6	2.4 ± 0.6	2.2 ± 0.6	1.8 ± 0.4	2.1 ± 0.7	<0.05
BE	1.8 ± 1.2	−01.2 ± 2.2	−02.6 ± 2.4	−05.0 ± 2.7	−07.5 ± 3.2	0.752
O_2 saturation (%)	62 ± 4	10 ± 5	5 ± 3	4 ± 1	4 ± 1	0.055
Ratio 2:30						
$ETCO_2$ (kPa)	5.2 ± 0.2	6.0 ± 0.3	6.0 ± 0.5	6.2 ± 0.4	6.3 ± 0.4	
Arterial blood gas						
pH	7.47 ± 0.03	7.33 ± 0.03	7.27 ± 0.03	7.24 ± 0.04	7.20 ± 0.03	
pCO_2 (kPa)	5.2 ± 0.4	7.0 ± 0.5	7.6 ± 0.4	7.9 ± 0.4	8.0 ± 0.7	
pO_2 (kPa)	11.7 ± 0.9	6.5 ± 1.1	6.5 ± 1.5	7.2 ± 1.5	7.3 ± 1.3	
BE	1.6 ± 1.6	0.1 ± 2.5	−2.2 ± 2.1	−3.9 ± 2.2	−6.2 ± 1.7	
O_2 saturation (%)	96 ± 1	67 ± 12	67 ± 15	69 ± 13	67 ± 12	
Oxygen content (ml dl^{-1})	11.3 ± 0.4	8 ± 1.3	8 ± 1.7	8 ± 1.5	8 ± 1.5	
Venous blood gas						
pH	7.39 ± 0.03	7.26 ± 0.03	7.20 ± 0.04	7.16 ± 0.05	7.12 ± 0.04	
pCO_2 (kPa)	6.0 ± 0.5	8.4 ± 0.9	9.2 ± 1.1	9.9 ± 1.0	10.5 ± 1.2	
pO_2 (kPa)	6.3 ± 0.6	3.1 ± 0.9	2.8 ± 0.8	2.9 ± 0.6	2.8 ± 0.4	
BE	1.5 ± 1.4	−1.1 ± 2.5	−3.1 ± 2.7	−4.3 ± 2.4	−5.7 ± 2.2	
O_2 saturation (%)	61 ± 3	16 ± 13	15 ± 11	13 ± 6	11 ± 5	

P values vs. ratio 2:30 using area under curve analysis.

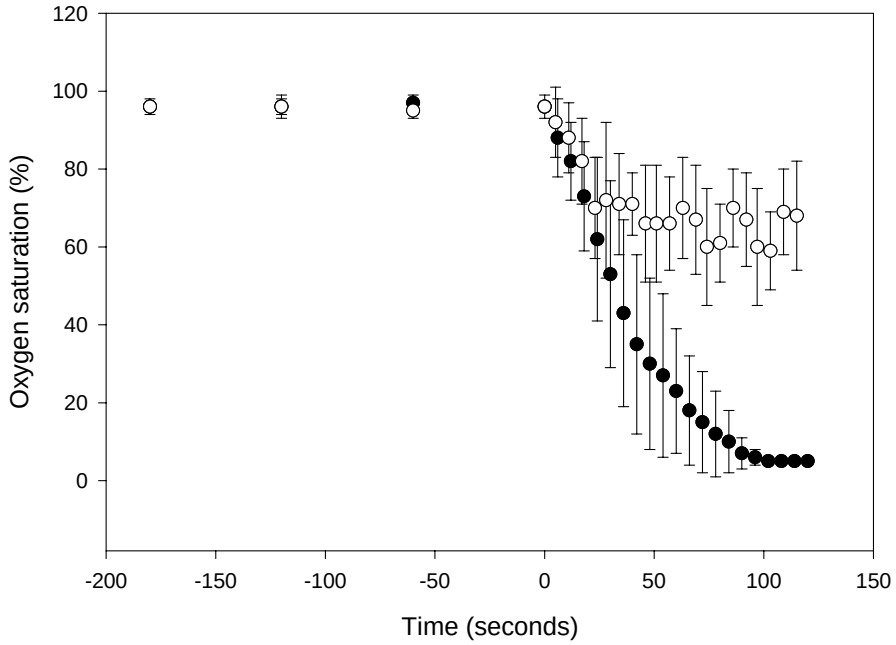

Fig. 1. Mean (±S.D.) arterial oxygen saturation (%) during the 3 min no-flow period and the initial 2 min of BLS for chest compressions only (●) and ratio 2:30 (○). End of no-flow period and start of BLS period is set to zero (0) seconds.

BLS with a ventilation:compression ratio of 2:30, a compression rate of 100 per minute and pausing 4.8 ± 0.2 s for delivery of two ventilations resulted in an average minute ventilation of 3.8 ± 0.3 l min^{-1}.

3.4. Oxygen delivery

During BLS, arterial oxygen content and cerebral oxygen delivery were significantly higher in the ventilated group than in the chest compressions only group (Table 2).

3.5. Outcome

Significantly more pigs ventilated during BLS achieved return of spontaneous circulation (ROSC) within the first 2 min (early ROSC) of ALS. While all except one compressions-only animal achieved ROSC before the experiment was terminated, the median time to ROSC was therefore shorter in the ventilated group (Table 4).

Table 4
Resuscitation outcome

	Compressions-only	Ratio 2:30
ROSC in <2 min	1 of 6*	6 of 6
ROSC total	5 of 6	6 of 6
Time to ROSC (min)	6.7 (5.4, 7.4)*	1.5 (0.8, 1.6)
Number of shocks	7 (5, 8)*	2 (1, 2)
Number of adrenalin doses	2 (2, 2)	1 (1, 1)

Time to ROSC and number of shocks are presented as median (25, 75 percentile).
* $P < 0.05$ vs. ratio 2:30.

4. Discussion

In this study, simulated mouth-to-mouth ventilation during 10 min of BLS after 3 min of untreated ventricular fibrillation resulted in better cerebral oxygen delivery and shorter time to ROSC in the following ALS period compared with chest compressions only. If chest compressions were administered alone, the arterial blood was in fact virtually desaturated within 1.5–2 min. This decline was significantly attenuated by the interposition of 2 ventilations with expired air following every 30th compressions.

For blood flow measurements a transit-time ultrasound flowmetry probe on the carotid artery and cerebrocortical laser-doppler flowmetry (LDF) were used. Both methods give continuous measurements which are of great advantage in unstable and dynamic situations. LDF is therefore also suitable for the study of blood flow dynamics during CPR [24,30]. It has the disadvantage of only giving a measurement from a very small area, and it was therefore felt important to combine it with the more global measurement of carotid blood flow. The radioisotope microsphere technique [31], previously used by our research group [26,32,33] only allows for a limited number of intermittent measurements. Brain tissue oxymetry allows for continuous measurement of brain tissue oxygen tension reflecting the combined effect of blood flow, arterial oxygenation and metabolic activity [34], but also measures from a very limited area. As we were primarily interested in blood flow dynamics LDF and carotid blood flow were chosen.

The necessity of ventilation during CPR has come under close scrutiny in recent years. Current experimental and clinical evidence seem to deemphasize the importance of

ventilation during the initial period of CPR, although the medical data on this issue are not altogether in agreement. Our results differ from the findings of three independent, well established laboratories that chest compressions only is as effective as chest compressions plus rescue breathing during the initial 6–12 min of CPR [5,6,18,19,35,36]. The major reason for the difference in results is probably the persistence of an open airway in the previous studies allowing for ventilation produced by chest compressions alone or in conjunction with spontaneous gasping.

We chose a model which we believe more closely mimics the situation in a supine, unconscious patient who tends to have an obstructed upper airway [37], allowing for exhalation in the compression phase but no inhalation in the decompression phase. Safar et al. have thus reported that chest compressions alone failed to produce any tidal volumes in humans with an unsupported head or airway [38,39]. In all 30 curarized humans with an unsupported head and no artificial airway, the tidal volume with chest compressions was zero. With the head in a backward tilted position the tidal volume was still zero in 16 of the 30 patients, while they achieved an average tidal volume of 156 ml per chest compression when an artificial airway was added. Furthermore, spontaneous gasping cannot be relied on to produce gas exchange in man [40,41]. This strongly indicates that adequate gas exchange and oxygenation cannot be achieved without assisted ventilation in human cardiac arrest victims. Therefore, in the present study, as in a more recently published trial by Kern et al. [7], the possible influence of a patent airway has been eliminated in order to enhance the physiological and clinical relevance of the reported data. As a cautionary note we are not aware of a study specifically testing the hypothesis that an obstructed airway in a cardiac arrest patient allows for exhalation in the compression phase, but no inhalation in the decompression phase. From other clinical circumstances it is well known however, that a supraglottic obstruction usually causes inspiratory, not expiratory stridor (opposite in contrast to an infraglottic obstruction which causes expiratory stridor).

In the current investigation no ventilation in the BLS phase was associated with a prolonged ALS phase, later ROSC, a higher dose of adrenaline and more defibrillation attempts. This is consistent with the observation by Idris et al. [42] that ventilation improves the success of cardiac resuscitation in pigs with VF. The improved resuscitability with assisted ventilation in the present study is probably due to the sustained tissue oxygen delivery and CO_2 removal. With compressions only the arterial oxygen saturation, and accordingly the oxygen content, were so low after 1.5–2 min (figure) that no more oxygen could be delivered to the tissues.

This observation on resuscitation success is consistent with a number of other studies showing that survival from cardiac arrest is influenced by blood acid–base balance and oxygenation. Both hypoxia and hypercarbic acidosis profoundly decrease the force of contraction of the myocardium profoundly, compromise the capability for successful defibrillation and adversely affect resuscitability [43–48]. Collectively, these cited experimental reports have also raised concern whether it is beneficial, safe, or advisable to ventilate cardiac arrest patients with the gaseous mixture exhaled by rescuers performing mouth-to-mouth ventilation. In the present study the arterial oxygen content stayed at 2/3 of normal when ventilating for 10 min with a gas mixture mimicking exhaled air, and the results indicate that mouth-to-mouth rescue breathing is preferable to chest compressions alone with an obstructed airway. In a prospective, observational study from Belgium survival from out-of-hospital cardiac arrest tended to be higher when bystanders correctly performed both mouth-to-mouth ventilation and chest compressions (16%, CI 13–19%) than when bystanders performed only chest compressions (10%, CI 7–14%) [41]. In a recent Swedish report the corresponding numbers were 9.7% of 8979 patients versus 6.8% of 278 patients [49].

While it was easier to resuscitate the ventilated pigs, all except one compressions-only pig eventually achieved ROSC. Even if it is assumed that only 1.5–2 min of BLS in this group provided any useful oxygen delivery before ALS was initiated, previous studies have shown that ROSC can be achieved in most pigs after 12 min even without any CPR [6,50].

In agreement with previous studies [51–53] there was no significant change in the arterial oxygen saturation during 3 min of untreated ventricular fibrillation, as the arterial tree functions more or less as an in vitro system with minimal gas exchange through the wall [54]. The near-total arterial deoxygenation within 1.5–2 min of chest compressions only CPR is consistent with data reported by Lesser et al. in a canine VF model where sternal compressions were commenced with the tracheal tube clamped in end expiration [51]. Kern et al. on the other hand documented a much slower decline in arterial oxygenation in the airway-obstructed compressions-only group [7]. Blocking the airway by merely clamping the tracheal tube retains air in the lungs as a reservoir, and this would explain the more sustained gas exchange in Kern et al's unventilated pigs.

The optimal ratio of chest compressions to ventilation during BLS is still unknown. Interrupting chest compressions for ventilation results in fewer chest compressions and can result in less blood flow per minute of CPR [7,14], and a higher ratio of compressions to ventilations might result in better oxygen delivery if it does not cause a relatively greater decrease in blood oxygen content. In the present study carotid and cerebral blood flow were not higher in the non-ventilated animals despite the fact that during 20% of the time was without there were no compressions in the ventilated group. It cannot be excluded that this is due to a type II statistical error as the cortical cerebral blood flow tended to be higher with compressions only ($P = 0.11$). On the other hand there was not even a trend towards a difference in coronary perfusion pressure.

It can be argued that the time for ventilation of a mean of 4.8 s with a ratio of 2:30 made that group come out

too favourably, as a recent report on lay rescuer CPR performance showed a mean break in chest compressions for rescue breathing of 16 s [14,17]. To compare the two groups in the present study it is more important to emphasise that even if the blood flow had been much higher with compressions-only, this would not have improved the oxygen delivery to the tissues as there was no oxygen left in the blood to be delivered.

Based on a theoretical analysis Babbs and Kern [21] recently suggested that a ratio of 2:30 would be ideal with breaks in chest compressions of 2.5 s per breath as in the present study. In a previous study of different ventilation:compression ratios we found oxygen saturation data supporting that a ratio near 2:30 might be optimal for standard, guidelines specified, CPR [22]. The present oxygen delivery data for 2:30 closely matched the values for ratio 2:15 in our previous study, which were significantly better than for 2:50. On the other hand Babbs and Kern on the other hand estimated that 2:60 would be ideal if 8 s per breath were required as in the studies mentioned above [14,17], but their mathematical model included a much better sustained arterial oxygen content with the longer periods of continuous compressions than we have found. This combined information does however give some indications that the ratio 2:30 might be suitable for study in a real life cardiac arrest situation.

5. Conclusion

In conclusion we believe that in cardiac arrest with an obstructed airway, pulmonary ventilation should be strongly recommended.

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References

[1] Gallagher EJ, Lombardi G, Gennis P. Effectiveness of bystander cardiopulmonary resuscitation and survival following out-of-hospital cardiac arrest. JAMA 1995;274:1922–5.
[2] Cummins RO, Eisenberg MS, Hallstrom AP, Litwin PE. Survival of out-of-hospital cardiac arrest with early initiation of cardiopulmonary resuscitation. Am J Emerg Med 1985;3:114–9.
[3] Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Part 3: adult basic life support. The American Heart Association in collaboration with the International Liaison Committee on Resuscitation. Circulation 2000;102:122–59.
[4] Becker LB, Berg RA, Pepe PE, et al. A reappraisal of mouth-to-mouth ventilation during bystander-initiated cardiopulmonary resuscitation. A statement for healthcare professionals from the Ventilation Working Group of the Basic Life Support and Pediatric Life Support Subcommittees, American Heart Association. Resuscitation 1997; 35:189–201.
[5] Berg RA, Kern KB, Hilwig RW, et al. Assisted ventilation does not improve outcome in a porcine model of single-rescuer bystander cardiopulmonary resuscitation. Circulation 1997;95:1635–41.
[6] Berg RA, Kern KB, Sanders AB, Otto CW, Hilwig RW, Ewy GA. Bystander cardiopulmonary resuscitation. Is ventilation necessary? Circulation 1993;88:1907–15.
[7] Kern KB, Hilwig RW, Berg RA, Ewy GA. Efficacy of chest compression-only BLS CPR in the presence of an occluded airway. Resuscitation 1998;39:179–88.
[8] Locke CJ, Berg RA, Sanders AB, et al. Bystander cardiopulmonary resuscitation. Concerns about mouth-to-mouth contact. Arch Intern Med 1995;155:938–43.
[9] Brenner BE, Kauffman J. Reluctance of internists and medical nurses to perform mouth-to-mouth resuscitation. Arch Intern Med 1993;153:1763–9.
[10] Ornato JP, Hallagan LF, McMahan SB, Peeples EH, Rostafinski AG. Attitudes of BCLS instructors about mouth-to-mouth resuscitation during the AIDS epidemic. Ann Emerg Med 1990;19:151–6.
[11] Brennan RT, Braslow A. Skill mastery in cardiopulmonary resuscitation training classes. Am J Emerg Med 1995;13:505–8.
[12] Thoren AB, Axelsson A, Holmberg S, Herlitz J. Measurement of skills in cardiopulmonary resuscitation—do professionals follow given guidelines? Eur J Emerg Med 2001;8:169–76.
[13] Morgan CL, Donnelly PD, Lester CA, Assar DH. Effectiveness of the BBC's 999 training roadshows on cardiopulmonary resuscitation: video performance of cohort of unforewarned participants at home six months afterwards. BMJ 1996;313:912–6.
[14] Assar D, Chamberlain D, Colquhoun M, et al. Randomised controlled trials of staged teaching for basic life support. 1. Skill acquisition at bronze stage. Resuscitation 2000;45:7–15.
[15] Eftestol T, Sunde K, Steen PA. Effects of interrupting precordial compressions on the calculated probability of defibrillation success during out-of-hospital cardiac arrest. Circulation 2002;105:2270–3.
[16] Berg RA, Sanders AB, Kern KB, et al. Adverse hemodynamic effects of interrupting chest compressions for rescue breathing during cardiopulmonary resuscitation for ventricular fibrillation cardiac arrest. Circulation 2001;104:2465–70.
[17] Chamberlain D, Smith A, Colquhoun M, Handley AJ, Kern KB, Woollard M. Randomised controlled trials of staged teaching for basic life support: 2. Comparison of CPR performance and skill retention using either staged instruction or conventional training. Resuscitation 2001;50:27–37.
[18] Berg RA, Wilcoxson D, Hilwig RW, et al. The need for ventilatory support during bystander CPR. Ann Emerg Med 1995;26:342–50.
[19] Noc M, Weil MH, Tang W, Turner T, Fukui M. Mechanical ventilation may not be essential for initial cardiopulmonary resuscitation. Chest 1995;108:821–7.
[20] Sanders AB, Kern KB, Berg RA, Hilwig RW, Heidenrich J, Ewy GA. Survival and neurologic outcome after cardiopulmonary resuscitation with four different chest compression-ventilation ratios. Ann Emerg Med 2002;40:553–62.
[21] Babbs C, Kern K. Optimum compression to ventilation ratios in CPR under realistic, practical conditions: a physiological and mathematical analysis. Resuscitation 2002;54:147.
[22] Dorph E, Wik L, Stromme TA, Eriksen M, Steen PA. Quality of CPR with three different ventilation: compression ratios. Resuscitation 2003;58:193–201.
[23] Eyre JA, Essex TJ, Flecknell PA, Bartholomew PH, Sinclair JI. A comparison of measurements of cerebral blood flow in the rabbit using laser Doppler spectroscopy and radionuclide labelled microspheres. Clin Phys Physiol Meas 1988;9:65–74.
[24] Gedeborg R, Silander HC, Rubertsson S, Wiklund L. Cerebral ischaemia in experimental cardiopulmonary resuscitation—comparison of epinephrine and aortic occlusion. Resuscitation 2001;50:319–29.

[25] Wenzel V, Idris AH, Banner MJ, Fuerst RS, Tucker KJ. The composition of gas given by mouth-to-mouth ventilation during CPR. Chest 1994;106:1806–10.
[26] Langhelle A, Stromme T, Sunde K, Wik L, Nicolaysen G, Steen PA. Inspiratory impedance threshold valve during CPR. Resuscitation 2002;52:39–48.
[27] Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Part 6: Advanced Cardiovascular Life Support. Circulation 2003;102:I86–I166.
[28] Part 6: advanced cardiovascular life support. Section 3: adjuncts for oxygenation, ventilation, and airway control. European Resuscitation Council. Resuscitation 2000;46:115–25.
[29] Matthews JN, Altman DG, Campbell MJ, Royston P. Analysis of serial measurements in medical research. BMJ 1990;300:230–5.
[30] Johansson J, Gedeborg R, Basu S, Rubertsson S. Increased cortical cerebral blood flow by continuous infusion of adrenaline (epinephrine) during experimental cardiopulmonary resuscitation. Resuscitation 2003;57:299–307.
[31] Heymann MA, Payne BD, Hoffman JI, Rudolph AM. Blood flow measurements with radionuclide-labeled particles. Prog Cardiovasc Dis 1977;20:55–79.
[32] Wik L, Naess PA, Ilebekk A, Nicolaysen G, Steen PA. Effects of various degrees of compression and active decompression on haemodynamics, end-tidal CO2, and ventilation during cardiopulmonary resuscitation of pigs. Resuscitation 1996;31:45–57.
[33] Sunde K, Wik L, Naess PA, Ilebekk A, Nicolaysen G, Steen PA. Effect of different compression—decompression cycles on haemodynamics during ACD-CPR in pigs. Resuscitation 1998;36:123–31.
[34] Kiening KL, Unterberg AW, Bardt TF, Schneider GH, Lanksch WR. Monitoring of cerebral oxygenation in patients with severe head injuries: brain tissue pO_2 versus jugular vein oxygen saturation. J Neurosurg 1996;85:751–7.
[35] Chandra NC, Gruben KG, Tsitlik JE, et al. Observations of ventilation during resuscitation in a canine model. Circulation 1994;90:3070–5.
[36] Tang W, Weil MH, Sun S, et al. Cardiopulmonary resuscitation by precordial compression but without mechanical ventilation. Am J Respir Crit Care Med 1994;150:1709–13.
[37] Safar P, Escarraga LA, Chang F. Upper airway obstruction in the unconscious patient. J Appl Physiol 1959;14:760–4.
[38] Safar P, Brown TC, Holtey WJ. Failure of closed chest cardiac massage to produce pulmonary ventilation. Dis Chest 1962;41:1–8.
[39] Safar P, Brown TC, Holtey WJ, Wilder RJ. Ventilation and circulation with closed-chest cardiac massage in man. JAMA 1961;176:574–6.
[40] Clark JJ, Larsen MP, Culley LL, Graves JR, Eisenberg MS. Incidence of agonal respirations in sudden cardiac arrest. Ann Emerg Med 1992;21:1464–7.
[41] Van Hoeyweghen RJ, Bossaert LL, Mullie A, et al, Calle P, Martens P, Buylaert WA. Quality and efficiency of bystander CPR. Belgian Cerebral Resuscitation Study Group. Resuscitation 1993;26:47–52.
[42] Idris AH, Becker LB, Fuerst RS, et al. Effect of ventilation on resuscitation in an animal model of cardiac arrest. Circulation 1994;90:3063–9.
[43] von Planta I, Weil MH, von Planta M, Gazmuri RJ, Duggal C. Hypercarbic acidosis reduces cardiac resuscitability. Crit Care Med 1991;19:1177–82.
[44] Tang WC, Weil MH, Gazmuri RJ, Bisera J, Rackow EC. Reversible impairment of myocardial contractility due to hypercarbic acidosis in the isolated perfused rat heart. Crit Care Med 1991;19:218–24.
[45] Yakaitis RW, Thomas JD, Mahaffey JE. Influence of pH and hypoxia on the success of defibrillation. Crit Care Med 1975;3:139–42.
[46] Tang W, Weil MH, Maldonado FA, Gazmuri RJ, Bisera J. Hypercarbia decreases effectiveness of electrical defibrillation during CPR. Crit Care Med 1992;20(Suppl):S24.
[47] Kerber RE, Sarnat W. Factors influencing the success of ventricular defibrillation in man. Circulation 1979;60:226–30.
[48] Idris AH, Wenzel V, Becker LB, Banner MJ, Orban DJ. Does hypoxia or hypercarbia independently affect resuscitation from cardiac arrest? Chest 1995;108:522–8.
[49] Holmberg M, Holmberg S, Herlitz J. Factors modifying the effect of bystander cardiopulmonary resuscitation on survival in out-of-hospital cardiac arrest patients in Sweden. Eur Heart J 2001;22:511–9.
[50] Berg RA, Kern KB, Hilwig RW, Ewy GA. Assisted ventilation during 'bystander' CPR in a swine acute myocardial infarction model does not improve outcome. Circulation 1997;96:4364–71.
[51] Lesser R, Bircher N, Safar P, Stezoski W. Sternal compression before ventilation in cardiopulmonary resuscitation. Prehospital Disaster Med 1985;1:239–41.
[52] Meursing BTJ, Zimmerman ANE, vanHeyst ANP. Experimental evidence in favor of a reversed sequence in cadiopulmonary resuscitation. J Am Coll Cardiol 1983;1:610.
[53] Tucker KJ, Idris AH, Wenzel V, Orban DJ. Changes in arterial and mixed venous blood gases during untreated ventricular fibrillation and cardiopulmonary resuscitation. Resuscitation 1994;28:137–41.
[54] Rahn H. Body temperature and acid–base regulation. Pneumonologie 1974;151:87–94. Review article.