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Alternative methods of mechanical Cardiopulmonary Resuscitation

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Abstract

Due to the relative ineffectiveness of standard resuscitation techniques, alternative methods have been explored for many years. The aim of new methods is to improve haemodynamics and increase survival rates. In spite of some encouraging haemodynamic results, all but one study failed to show an increase in long-term survival rates with an alternative method in a convincingly large group of patients (hospital discharge without neurological damage, and 1-year survival). In this study active compression–decompression resuscitation (ACD-CPR) increased long-term survival compared to standard-CPR. The results from certain individual studies, which showed a significant increase in short-term survival rate, could not be reproduced in other trials. This may be attributed in part to the fact that the alternative methods are not significantly superior, but also due to logistical and statistical problems in the conduct of the studies and differences in application within and between the study sites. ACD-CPR has been the most studied method amongst the alternatives and can be recommended for patients with asystole in centres with special training and where outcome quality is regularly verified and evaluated. © 2000 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Cardioplumonary resuscitation; New methods; Survival rate

1. Introduction

In spite of enormous logistic improvements, the majority of the patients suffering cardiocirculatory arrest outside the hospital [1–5] still die. Even in areas with well-developed rescue systems, hospital discharge rates of only 15–20% can be achieved. In large conurbations with many multi-storey buildings and slums, and in rural areas, the chance of surviving a circulatory arrest occurring outside the hospital is generally < 5%, because rescue staff arrive too late and treatment is delayed [6,7]. Outcome in these patients is influenced by the effectiveness of basic cardiopulmonary resuscitation. During resuscitation, the maximum coronary perfusion achieved is 15–20%, and the maximum cerebral perfusion is 25–30%, compared with the spontaneously beating heart [8–10]. The higher the organ perfusion pressure, the higher the chance of survival following cardiopulmonary resuscitation [11–14].

In an effort to increase the effectiveness of external chest compressions, the standard technique has been modified frequently: the compression rate has been increased from 60 to 80–100 per min, the duration of compression and relaxation should each be 50% of the duration of the cycle, and the compression depth should be between 3.8 and 5 cm [15–17]. Nevertheless, compared with a spontaneously beating heart, a maximum cardiac output of 30% only can be achieved with external chest compression without simultaneous vasopressor therapy [18]. This has led to an intensive search for alternative methods of mechanical resuscitation (Table 1).

2. Pathophysiological principles

The objective of cardiopulmonary resuscitation is to ensure an oxygen supply to the heart and

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brain sufficient to restore conditions for a return of spontaneous circulation. The chance of survival is influenced decisively by the coronary and cerebral perfusion pressures generated by chest compressions [10–13]. Improved blood circulation during resuscitation produces higher organ perfusion pressure [10,13,19,20]. Animal experiments show that a myocardial blood flow of more than 20 ml/min per 100 g of tissue is required to cover the oxygen need of the heart and to achieve successful cardiac resuscitation [8]. To avoid irreversible cerebral damage, cerebral blood flow should not fall below 16 ml/min per 100 g of brain tissue [19].

Two different theories attempt to explain the mechanism of blood flow during cardiopulmonary resuscitation [18].

The heart pump theory is based on the concept that the heart is compressed between the spinal column and the sternum during the chest compressions [21]. Direct cardiac compression is characterized by a reduction in ventricle size with ventricular filling at the end of the compression phase. At the same time pressure in the aorta is increased. During the relaxation phase, the pressure in the aorta falls, and the ventricles fill [22–24]. In 1976, the heart pump theory was questioned by Criley, having observed cough resuscitation [25]. The rhythmic changes of intrathoracic pressure induced during coughing generated a cardiac output, which was sufficient to preserve consciousness.

In 1980 [9], a new mechanism was described, which was thought to be responsible for forward blood flow during closed chest compression. In this thoracic pump mechanism, external pressure on the chest causes an increase in intrathoracic pressure without direct compression of the heart [9,26]. The increase in intrathoracic pressure is evenly distributed over all heart chambers and intrathoracic vascular structures. A pressure gradient towards the aorta is generated resulting in forward blood flow. When the chest is released, the intrathoracic pressure falls below the pressure of the extrathoracic venous system, and blood flows passively into the venous vessels in the thorax. In the concept of this mechanism, the heart does not play an active role, but is considered as a passive conduit, while the lungs represent the reservoir from which the blood is extruded by the chest compressions [9,26].

Alternative methods of cardiopulmonary resuscitation, such as simultaneous compression and ventilation, vest resuscitation and cough resuscitation, show that pressure differences in the thorax are relevant for forward flow of blood during resuscitation. Thus, these methods support the thoracic pump theory. At the present time we cannot clearly determine which of the two theories is principally responsible for blood flow during cardiopulmonary resuscitation. In patients with a large thoracic volume, the thoracic pump mechanism is likely to be the principle factor. In patients with a small thorax or when high compression force is used, the heart pump effect is responsible for forward blood flow [18].

3. Alternative methods of the cardiopulmonary resuscitation

3.1. Cough resuscitation

Cough resuscitation generates substantial intrathoracic and intra-abdominal pressure differences. Criley [25] describes the phases responsible for the intrathoracic pressure variations and, blood flow during cough resuscitation: in the first phase, deep inspiration generates a negative intrathoracic pressure, followed by closure of the glottis. The second phase comprises compression of the thoracic and abdominal wall muscles with continued closure of the glottis resulting in a sudden increase of abdominal and thoracic pressure. In the third phase, the glottis opens, air is forced out of the respiratory tract, and the thoracic and abdominal pressures suddenly fall to atmospheric or subatmospheric level.

Table 1
Alternative methods of mechanical cardiopulmonary resuscitation

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Cough resuscitation

Simultaneous thorax compression and ventilation (SCV-CPR)

Thorax compression in combination with abdominal compression
· Continuous
· Interposed (IAC-CPR)

Pneumatic vest resuscitation

Active compression–decompression resuscitation (ACD-CPR)

3.1.1. Animal experiments

In 1985, Niemann [27] imitated the effect of cough resuscitation in a dog model by tying an inflatable vest around the thorax and abdomen. This vest is intermittently inflated with a pressure between 100 and 200 mmHg at a frequency of 50 per min. Ventilation is performed synchronously with vest insufflation applying a tidal volume of 15 ml/kg. Compared with standard resuscitation, there was a significant difference in 24-h survival of the animals in favour of cough resuscitation. With respect to systolic aortic pressure, right arterial pressures, mean aortic pressure and blood gas analysis, there were no differences between the two groups. The higher rate of survival in cough resuscitation can be explained by the significantly higher diastolic coronary perfusion pressure (23 vs. 6 mmHg). In the course of further studies [28,29], cough was produced by the stimulation of the cervical vagus nerves after induced ventricular fibrillation. With these experiments, it was shown that during ventricular fibrillation an aortic pressure could be generated which corresponds to normal and carotid flow reached almost 80% of a spontaneously beating heart.

3.1.2. Clinical studies

In the catheter laboratory, patients with witnessed ventricular fibrillation were asked to cough frequently. By means of the cough, intrathoracic pressure variations were generated, sufficient to provide organ perfusion to maintain consciousness for up to 40 s. A pressure of more than 100 mmHg was measured in the central aorta and all patients treated with this method were successfully resuscitated and discharged from the hospital [29].

Cough resuscitation can be considered the prototype of the thorax pump model of resuscitation, because blood flow results entirely from changes in the thoracic, and, to a small extent, abdominal pressure. Rhythmic coughing ensures effective systemic blood flow during ventricular fibrillation without direct chest compressions. The main limiting factor for cough resuscitation is the short period of time (≈ 40 s) that this measure is effective while the patient is awake, responsive, and co-operative. Cough resuscitation in the very early phase of cardiac arrest, while the patient remains conscious, has been included in international resuscitation recommendations. So far, no device able to simulate cough resuscitation during human resuscitation has been developed.

3.2. Simultaneous chest compression and ventilation with high airway pressures during cardiopulmonary resuscitation (SCV-CPR)

The observation that high intrathoracic pressures, generated during cough resuscitation, led to a reasonable cerebral blood flow inspired Chandra and her colleagues [30] to suggest that pressure gradients and blood flow during cardiopulmonary resuscitation could be significantly increased by high intrathoracic pressures achieved by simultaneous chest compression and ventilation.

3.2.1. Animal experiments

In dog experiments, SCV-CPR led to a significant increase of blood flow in the carotid and coronary arteries compared with standard resuscitation [31,32]. There was no increase in side effects, such as barotrauma. In another study, SCV-CPR, using a frequency of 30/min and a maximum airway pressure of 80 mmHg, produced a significant increase in circulation to the brain, heart, and kidneys compared with standard resuscitation [33]. Experiments with dogs of various sizes and with different compression surfaces showed that in absence of a direct cardiac massage, SCV-CPR significantly increases cardiac output. No increase in cardiac output compared with standard resuscitation occurs in animals in which direct cardiac compression produces the main effect of resuscitation. These experimental results were reproduced in a further experiment performed with small pigs [34,35].

3.2.2. Clinical studies of SCV-CPR

In the first study on human beings SCV-CPR was performed at a frequency of 40/min. and a compression duration of 60% of the cycle with airway pressures between 60 and 110 cmH$_2$O [36]. In this study, SCV-CPR significantly increased mean systolic pressure and blood flow index in the carotid artery compared with control values. The effects of SCV-CPR on coronary perfusion pressure were examined in a further study of 20 patients who suffered a circulatory arrest outside the hospital and were subsequently treated in the emergency ward [37]. In 5 of the 20 patients SCV-CPR was applied after standard resuscita-

tion had failed. These patients did not show significant changes in systolic aortic pressure and coronary perfusion pressure. A study performed with 994 patients examined the influence of SCV-CPR on hospital admission and discharge rates [38]. It was a prospective examination, in which the patients were randomized to receive SCV-CPR or standard resuscitation. Both the hospital admission rate (26.2 vs. 19%) and the hospital discharge rate (10.6 vs. 5.9%) were significantly higher in the group treated with standard resuscitation. The neurological outcome was the same for both groups.

In conclusion, simultaneous compression–ventilation resuscitation did not show a uniform improvement in haemodynamic values. In a preclinical study with a sufficient number of patients, SCV-CPR was inferior to standard resuscitation in primary and secondary survival.

3.3. Chest compression in combination with abdominal compression

The first description of abdominal compression in resuscitation was published in 1976 [39]. Two forms of abdominal compression can be distinguished:

1. continuous abdominal compression by means of a circumferential vest,
2. interposed abdominal compression (IAC-CPR), i.e. chest compression alternates with abdominal compression.

3.4. Resuscitation with continuous abdominal compression

If standard resuscitation methods with and without continuous abdominal compression are compared, no significant differences between the two test groups are found [31]. The haemodynamic data showed that the abdominal compression led to a significant increase of the systolic aortic pressure, while diastolic pressure remained unchanged.

3.5. Interposed abdominal compression with simultaneous thorax relaxation (IAC-CPR)

When abdominal compression is applied during relaxation of the chest, intrathoracic pressure and systemic blood flow can be increased [18].

3.5.1. Animal experiments

Kimmel [40] compared standard resuscitation with abdominal compression and IAC-CPR. He was able to show that IAC-CPR had significant advantages over chest compressions alone and over a combination of chest compressions and continuous abdominal countercompression. The blood flow index in the carotid artery was increased by 77% (from 13% with continuous compression to 23% with interposed abdominal compression), and cardiac output index increased by 65% (from 7.8 with continuous compression to 12.5% with interposed compression). With mechanical automatic chest compression and interposed abdominal compression, the cardiac output, systolic and diastolic blood pressures, and coronary perfusion pressure were increased [41,42]. While an improvement of cerebral blood flow by IAC-CPR compared with standard resuscitation could be identified, no improvement in myocardial blood flow could be achieved. In a pig model, Lindner [45] compared the effectiveness of intra-abdominal counterpulsation versus standard resuscitation both in pigs asphyxiated to cardiac arrest and in induced ventricular fibrillation. None could be revived using standard resuscitation, but all animals could be resuscitated by IAC-CPR. The end-diastolic arteriovenous pressure difference, which strongly correlates with coronary blood flow, was significantly higher with interposed abdominal compression during resuscitation from both forms of arrest. With asphyxial arrest, the pressure increased from 9.8 mmHg during standard resuscitation to 32.1 mmHg during abdominal countercompression. With pigs with ventricular fibrillation, this pressure gradient increased from 12.4 mmHg during standard resuscitation to 34.1 mmHg during abdominal countercompression.

3.5.2. Clinical studies

The first haemodynamic measurements using IAC-CPR performed with human beings occurred in 1984 [46]. In this study, the mean arterial pressure was increased by 50% (from 26 to 39 mmHg) with IAC-CPR. In a further clinical study [44] of 14 patients with circulatory arrest, IAC-CPR increased diastolic aorta pressure to 43 compared with 25 mmHg during standard resuscitation. A prospective randomized study of 143 patients with in-hospital circulatory arrest with primary asystole

or electromechanical dissociation [47] compared standard resuscitation with IAC-CPR. The number of patients in which spontaneous circulation could be restored, was significantly higher in the study group (49 vs. 28%). At 24 h after resuscitation, more patients in the abdominal counterpulsation group survived compared with the control group (33 vs. 13%). The long-term success or the hospital discharge rate were not examined in this study. Autopsy revealed no differences between the two methods with respect to the frequency of organ damages. These encouraging results were reproduced in another study of 103 patients in New Jersey with regard to long-term survival rate. In this study, 25% of the patients treated with standard resuscitation and additional abdominal compression were discharged from the hospital, compared with 7% treated with standard resuscitation [48]. There were no differences in side effects. An out-of-hospital study [49] of 291 patients, however, did not show a significant difference between standard resuscitation and abdominal counter-compression in primary survival rates (31% in the control group vs. 28% in the study group).

3.6. Pneumatic vest resuscitation

3.6.1. Method

When applying this technique, a vest is put around the entire thorax. This vest is rhythmically inflated by an external control device intermittently compressing the thorax. Frequency, pressure, and compression duration can be exactly adjusted. The defibrillator electrodes must be fixed to the thorax prior to application of the vest [50,51].

3.6.2. Mechanism of action

In contrast to standard resuscitation, vest resuscitation applies high pressure which is evenly distributed on the entire thorax. If such a pressure was exercised over a small area, it would certainly result in a substantial increase in complications (lung contusion, organ ruptures) [50–52].

3.6.3. Animal experiments

Halperin tested his vest resuscitation system for the first time in 1986 in eight dogs applying a maximum vest pressure of 380 mmHg [52]. In these studies, the myocardial blood flow during resuscitation corresponded to the flow before cir-

culatory arrest, and cerebral blood flow was even higher than before circulatory arrest. In the autopsies performed after resuscitation, however, three out of eight dogs showed severe lung and liver trauma. In the second part of the study, the maximum vest pressure was limited to 280 mmHg; no severe trauma was observed, but the blood flows were significantly lower. In the next part of the study, Halperin compared vest resuscitation with standard resuscitation applying conventional and higher compression pressures to the sternum. During standard resuscitation with normal sternal compression, myocardial and cerebral blood flows were significantly lower than with vest resuscitation. With a high sternal compression pressure applied during standard resuscitation, blood flows were comparable to the vest resuscitation, but dogs in these groups had more severe rib and liver injuries. All animals resuscitated with the vest survived the first 24 h. Significantly less animals survived in the groups of dogs revived with the two standard resuscitation methods. In the pig model, there were no differences between vest and standard resuscitation with respect to myocardial and cerebral blood flows [52]. Kern [53] compared three resuscitation methods, namely standard resuscitation, SCV-CPR and vest resuscitation. SCV-CPR and vest resuscitation produced significantly higher systolic aortic and right arterial pressures, compared with standard resuscitation. SCV-CPR also showed significantly higher diastolic aortic pressure compared with vest and standard resuscitation. No significant differences between the three resuscitation methods could be determined with respect to coronary perfusion pressure, short-term and 24-h survival rates, and neurological outcome in surviving animals [43,53].

3.6.4. Clinical studies

In a study comprising two phases, Halperin examined the effects of vest resuscitation in patients on aortic and right arterial pressures and patient survival rate [54]. In phase 1, the pressure values were measured after an average of 42 min of standard resuscitation. These patients showed a significant increase in the maximum aortic pressure from an average of 78–138 mmHg and an increase of the coronary perfusion pressure from 15 to 23 mmHg after the application of vest resuscitation. In spite of the prolonged period of standard resuscitation prior to application of vest resuscitation, spontaneous circulation was restored

in 4 out of 29 patients. In phase 2 of the study, 34 patients were randomly allocated to standard resuscitation or vest resuscitation after unsuccessful standard resuscitation. The number who achieved a return of spontaneous circulation and survived for 6 and 24 h were higher in those allocated to vest resuscitation. Due to the small number of patients, the results were not statistically significant. None of the patients survived to leave hospital.

Interposed abdominal compression and vest resuscitation may be considered as promising alternative resuscitation methods. Animal experiments and measurements on patients have shown an improvement in haemodynamics with these methods. In-hospital clinical studies have also verified better resuscitation results. To date, an improvement in survival rates has not been proven in prehospital studies.

3.7. Active compression–decompression resuscitation (ACD-CPR)

The principle of active compression–decompression resuscitation was first described by Lurie and his colleagues [55] in 1989. A patient collapsed at home and was successfully resuscitated by his wife using a toilet plunger made of rubber with a wooden handle. At first, no attention was paid to this resuscitation method until the same patient collapsed again at home months later and suffered a circulatory arrest. The son remembered the toilet plunger. As his mother had done, he was able to successfully revive his father using this device and when the rescue team arrived, the patient had already regained consciousness.

3.7.1. Method
ACD-CPR is performed with a manually operated pressure–suction-pump. At the first compression, this pump adheres to the thorax, which is then expanded by an upward thrust on the handle of the pump. Compression is performed through a plate located in the pump and rhythmically alternates with active decompression [56–58].

3.7.2. Mechanism of action
As with standard resuscitation, the mechanisms which are responsible for the blood flow during resuscitation with ACD-CPR are very complex and cannot be imitated with a model. During compression, there is an increase of intrathoracic pressure and a certain degree of direct cardiac compression which both contribute to the blood flow from the thorax [57,58]. During active decompression a pronounced negative intrathoracic pressure is generated. Thus, the intrathoracic pressure differences are substantially higher than with standard resuscitation. With each compression, the rapid increase of intrathoracic pressure causes arterial blood flow from the thorax, and during decompression the rapid decrease of intrathoracic pressure causes venous blood to flow back into the chest resulting in significantly higher thoracic blood volume [57–59]. After active decompression there is more effective compression and a reduction in coronary vascular resistance which result in improved blood flow to the deep coronary bed as well as to the systemic system. The coronary and the systemic blood flow during compression depend, however, on many variables, such as thorax compliance, the volaemic state of the patient, myocardial function, and the power exercised during compression. The amount of negative intrathoracic pressure generated during ACD-CPR depends upon the degree of obstruction of the airway, on the quality of the decompression, on thorax compliance, and, of course, on adhesion of the suction pump to the chest. These factors may cause differences in the effectiveness of this new form of resuscitation [55,57,60,61]. Echocardiographic studies verify these hypotheses: they show that ACD-CPR does significantly increase blood flow through the mitral valve, backflow into the thorax, to the heart, and between the ventricles. A clear increase of left ventricular volume after decompression reflects the effectiveness of venous backflow to the heart. In various studies, the stroke volume increased by 17–85% with ACD-CPR [61,63].

3.7.3. Animal experiments (Tables 2 and 3)
The haemodynamic advantages of ACD-CPR were first described by Cohen [57,58]. In this study, significantly increased coronary perfusion pressure, systolic arterial pressure, intracranial blood flow, endtidal carbon dioxide, and timed vital capacity could be measured in a rabbit model with induced ventricular fibrillation. In further haemodynamic studies, significant increases of systolic, mean, and diastolic aortic pressures ranging from 11 to 83% compared with standard resuscita-

Table 2
ACD-CPR: haemodynamic results

	Cohen (58)	Lindner (67)	Rivers (69)	Shultz (65)	Chang (60)
Coronary perfusion-pressure (mmHg)		Without adrenaline			
ACD-CPR	$18 \pm 11*$	26 (21; 31)*	$16,1 \pm 9,5*$	$22,6 \pm 9*$	
S-CPR[a]	8 ± 6	18 (16; 23)	$13,2 \pm 8,2$	$19,3 \pm 8$	
Systolic Aortic pressure (mmHg)					
ACD-CPR	$68 \pm 19*$	80 (59; 86)*			$71 \pm 9*$
S-CPR	44 ± 11	62 (48; 70)			59 ± 8

* $P < 0.05$ vs. S-CPR.
[a] ACD-CPR, active compression–decompression CPR; S-CPR, standard resuscitation method.

tion were found [61,62,64,65]. ACD-CPR increased mean carotid blood flow by 22% and regional tissue blood flow to the brain [66]. Lindner [67] found a significant increase in myocardial and cerebral blood flow during ACD-CPR in a pig model. These differences in the organ circulation did, however, not occur in conjunction with high-dose adrenaline. In another animal model, ACD-CPR did not turn out to be superior to standard resuscitation [68].

3.7.4. Clinical studies

The first studies with human beings were performed after standard resuscitation had failed, i.e. a long time after the onset of circulatory arrest. Cohen [56,57] examined ten patients who were then randomly resuscitated with ACD or with the standard technique. The ACD-CPR method was able to double endtidal carbon dioxide tension, to increase transmitral flow by a factor of 2.5, and to increase the average femoral arterial pressure from 52.5 to 88.9 mmHg. Shulz [65] has examined cardiopulmonary haemodynamics during ACD resuscitation in 21 patients after defibrillator implantation. In these patients, the arterial and coronary perfusion pressure significantly increased during ACD resuscitation. Another group [69] examined 17 patients who had been admitted to hospital after unsuccessful resuscitation outside hospital. These patients were alternately, at 5-min intervals, resuscitated with standard resuscitation or ACD-CPR. This group of patients also showed a significant increase in coronary perfusion pressure with ACD-CPR.

3.7.5. Endtidal carbon dioxide tension (ET pCO₂)

Endtidal carbon dioxide tension rises with an increase of the cardiac output [70–75]. This value also depends, however, on ventilation volumes and carbon dioxide production from the tissue [76–79]. Most haemodynamic studies showed a significant increase of ET CO_2 concentration or ET pCO_2 during ACD resuscitation [56,61,67,80]. A prospective randomized study with 120 prehospital patients examined the effect of ACD-CPR on ET pCO_2 compared with standard resuscitation. There were no differences between the study groups, but the ET pCO_2 was a reliable marker for return of a spontaneous circulation [81].

3.7.6. Survival rate after resuscitation

Three studies [56,82,83] have compared the survival rate after ACD or standard resuscitation performed in the hospital randomly (Table 4). Two of these studies showed a significant increase in return of spontaneous circulation and in 24-h survival rate. However, the hospital discharge rate did not show any differences between the two study groups. Cohen [56] also observed an improvement in neurological performance after re-

Table 3
ACD-CPR: myocardial and cerebral blood flow

	Chang (60)	Lindner (67)
Myocardial blood-flow (ml/min per 100 g)		
ACD-CPR	$30 \pm 18*$	30 (9; 46)*
S-CPR[a]	22 ± 13	14 (7; 30)
		without adrenaline
Cerebral blood-flow (ml/min per 100 g)		
ACD-CPR	$14 \pm 6*$	30 (21; 39)*
S-CPR	10 ± 7	15 (10; 26)
		without adrenaline

* $P < 0.05$ vs. S-CPR.
[a] ACD-CPR, active compression–decompression CPR; S-CPR, standard resuscitation method.

Table 4
ACD-CPR: survival rates after in-hospital resuscitation

	Tucker (82)	Cohen (56)	Stiell (83)
Number of patients			
ACD-CPR[a]	25	29	405
S-CPR	28	33	368
ROSC[b]			
ACD-CPR (%)	60*	62*	
S-CPR (%)	32	30	
Short term survival rates			
ACD-CPR (%)[a]	48*	45*	34.6
S-CPR (%)	21	9	35.1
Discharge survival rates			
ACD-CPR (%)[a]	24	7	10.4
S-CPR (%)	11	0	11.4

* $P < 0.05$.
[a] ACD-CPR, active compression–decompression CPR; S-CPR, standard resuscitation method.
[b] ROSC, return of spontaneous circulation.

suscitation, measured by means of the Glasgow Coma Score. A further study could not reproduce these results: there were no differences in short- and long-term results (Table 4).

The first study outside hospital was performed by Lurie [84]. One hundred and thirty patients with circulatory arrest occurring outside the hospital were randomly allocated to ACD resuscitation ($N = 53$) or to standard resuscitation ($N = 77$). Within the entire cohort of patients, there was a trend in favour of ACD-CPR for return of spontaneous circulation and admission to the intensive care unit with improved neurological performance. A significant difference in short-term survival was found for those patients in the ACD-CPR group who were resuscitated within the first 10 min after the collapse. A trial performed in France [85] has shown increased short-term survival rates and in a second study significantly improved hospital discharge rate without neurological deficit (6 vs. 2%) and 1-year-survival rate (5 vs. 2%) in the ACD group [92]. All other prehospital studies, comparing standard resuscitation with ACD-CPR, showed only an improved short-term survival or no differences between the two methods [83,86–91,93] (Table 5). Relevant side effects of the methods were only described in one study [91]; in all other studies, the complication rate was comparably low for both methods.

A combined analysis [94], which analyzed individual data from almost 3000 patients in a common database, showed a significant increase in 1-h survival rate but not in hospital discharge rate (Table 6). However, a χ-square trend test (Table 7), which connects short- and long-term survival parameters, showed a significantly increased overall survival rate. In subgroup analyses patients with primary asystole were those who gained most from ACD-CPR. The authors concluded from the combined analysis that ACD-CPR is a reliable alternative resuscitation method, which can be recommended in centres with a rigorous training program and regularly verified outcome quality.

A *resuscitation valve*, designed to improve the effectiveness of the ACD-CPR prevents gas flow through the airways during the decompression phase. During the compression phase, the valve immediately opens allowing unhindered passive expiration. This valve is inserted into the ventilation circuit between tube and self-inflating bag. A silicone diaphragm located in the valve blocks the gas flow when pressure in the circuit falls below atmospheric. When the airway is obstructed by the valve during the decompression, the negative intrathoracic pressure is increased. Consequently, venous return to the heart rises, and circulation to vital organs is improved. Animal experiments have shown that ACD-CPR in combination with the valve may improve circulation in heart and brain by 50%, compared to ACD-CPR without the valve [95]. This method is currently being further assessed in several centres.

3.8. Other techniques

Phased chest and abdominal compression–decompression CPR and minimally invasive direct cardiac massage (MIDCM) are other new techniques which had been evaluated in some animal studies and in clinical studies with small patient numbers.

Phased chest and abdominal compression–decompression CPR combines ACD-CPR with IAC-CPR using two piston suction cups positioned on the chest and the abdomen. Compared to standard CPR improved haemodynamic and outcome parameters had been demonstrated in a small animal study [101]. In a prehospital study the new CPR method was found to be feasable and associated with less injuries. No significant differences in

Table 5
ACD-CPR: survival rates in prospective preclinical studies

	Schwab (89) Fresno	Schwab (89) San Francisco	Lurie (84)	Stiell (83)	Mauer (87)	Plaisance (85)	Plaisance (92)	Luiz (93)	Nolan (90)
Number of patients									
ACD-CPR[a]	117	297		501	106	254	373	26	267
S-CPR[a]	136	310		510	114	258	377	30	309
ROSC[b]									
ACD-CPR (%)	17	19			51	45*	39	38.5	23.2
S-CPR (%)	20	21			59	30	29	40	20.7
Short-term survival									
ACD-CPR (%)	16	13.5	18	18.2	33	33*	31	n.u.	13.8
S-CPR (%)	20	14.5	16	16.5	33	24	31	n.u.	13.6
Discharge rate									
ACD-CPR (%)	5	4.7	23	4.6	16	5*	6*	11.5	6
S-CPR (%)	7	5.5	17	3.7	14	2	2	13.3	4.8

* $P < 0.05$.

[a] ACD-CPR, active compression–decompression CPR; S-CPR, standard resuscitation method.

[b] ROSC, return of spontaneous circulation.

Table 6
ACD-CPR combined analysis: survival rates after prehospital resuscitation

	ACD-CPR[a]	S-CPR[a]
Number of patients	1410	1456
1-h survival rate	336 (24%)*	99 (7%)
Discharge survival	300 (20%)	85 (5%)

* $P < 0.05$ vs. S-CPR.
[a] ACD-CPR, active compression–decompression CPR; S-CPR, standard resuscitation method.

Table 7
ACD-CPR combined analysis: survival rates after prehospital resuscitation (chi-squared-test for trend[a])

	Death within 1 h	Death in hospital	Discharged
ACD-CPR (N)	1074	237	99
S-CPR[b] (N)	1156	215	85

[a] Test for trend, $P < 0.05$; χ^2 test: 3.97.
[b] ACD-CPR, active compression–decompression CPR; S-CPR, standard resuscitation method.

short- and long-term survival rates were found [102].

MIDCM produces blood flow by cyclic cardiac compression and relaxation with the help of a pocket-size plunger-like device inserted via a small thoracic incision directly over the left ventricle. In animal experiments this technique created organ perfusion pressures comparable to conventional open chest cardiac massage [103,104].

Both techniques need further clinical investigation and a corresponding training program prior to clinical application.

4. Discussion

Over the past decade certain alternative resuscitation methods have been shown to improve coronary and cerebral perfusion pressures and blood flow during resuscitation in animal experiments. However, the transfer of these positive laboratory studies to clinical routine has turned out to be difficult. At present, in multiple test sites all but one study failed to show an increase in long-term survival rates (hospital discharge without neurological damage) with an alternative method in a convincingly large group of patients. However,

important insight has been gained by analysis of the clinical experience in many of the studies. Re-analysis should help in the evaluation of current and future devices.

The alternative method which has been studied most intensively is active compression–decompression resuscitation. Further analysis of experience with ACD-CPR illustrates the challenges and future direction needed to improve the assessment of new CPR techniques. In the majority of the animal experiments and in haemodynamic studies with patients, arterial pressure, cerebral perfusion pressure and cerebral and myocardial blood flow, are significantly improved with this method. A significant increase of the endtidal carbon dioxide tension and timed vital capacity has also been observed with ACD resuscitation. In-hospital clinical studies showed initial improved resuscitation results. Short-term survival after out-of-hospital cardiac arrest has been found to be improved in some centers but not others. Long-term survival rates after prehospital use improved in only one center. However, most studies were underpowered and hospital discharge rate was not the primary study endpoint.

There are many potential reasons for these inconsistent results. First, standardized conditions, which can be achieved in a laboratory and in animal experiments, cannot be maintained with the studies in the hospital and even more in the prehospital environment. Secondly, clinical study sites are often different, making comparisons difficult. In one center, for example, the new method may be applied on arrival of the first tier personnel, whereas in another center the treatment may begin with the arrival of the second tier of paramedics or emergency physicians. Similarly, the time between arrest and initiation of the advanced life support is of importance.

The level of qualification of prehospital providers and their motivation can substantially influence study results [96–98]. When the first ACD-CPR studies were performed, there was no standardized training and the application of the method substantially differed within and between the individual study centers. The first training guidelines and recommendations were only prepared and published in 1995 and at that time the data collection in most studies had already reached an advanced stage [99,100]. In one study center, in Paris [85,92], ACD-CPR was introduced to prehospital providers more than 2 years before

beginning the clinical trials. This meant that these providers had already had long and intensive training. In contrast, resuscitation in the Canadian study [83] was performed during transport. This led, especially with ACD-CPR, to deterioration of resuscitation quality and, thus substantially influenced the study result.

Patient diversity is another important difference between the ACD-CPR study sites. Differences in the initial heart rhythm is important. In patients with ventricular fibrillation, the chance of survival is mainly determined by early defibrillation. In contrast, patients with asystole or electromechanical dissociation (EMD) gain from good perfusion during cardiopulmonary resuscitation. Both in the French study [85,92] and in the combined analysis of all patient data [94], analysis of the subgroup of patients in asystole and EMD revealed a significant increase probability of survival. These differences between the patients and various treatment strategies during the pre-and inhospital phase further complicate the evaluation of the device.

Perhaps the most important issue, however, relates to selection of an endpoint. The question must be asked if the demonstration of improved haemodynamics is sufficient to evaluate a new technique? Alternatively, should longer-term endpoints, such as an increase in hospital discharge rates, also be evaluated? With the exception of the Paris study, none of the prehospital studies examining the alternative form of resuscitation, were designed to demonstrate a significant long-term result in terms of the number of patients (study power). The largest single study was performed in Canada with a total of 1011 patients [83]. However, when survival rates are low, very large numbers of patients are needed to identify differences between different techniques. In a study with a new method, which is thought to increase long-term survival from 5 to 7.5% (i.e. by 50%), a significant result ($P < 0.01$) with a probability of 95% can only be expected with 7000 patients (3500 per group). These high case numbers can only be achieved in large-scale, multicentre studies where the quality of the individual data is often significantly lower than in monocentre studies. In view of this problem, a combined analysis was performed, comparing ACD-CPR with the standard method. In this study, all available individual data from the prospective prehospital studies were summarized in a database. The combined analysis

study showed a significant increase in 1-h survival with ACD-CPR. The clearest differences occurred in patients with asystole. The hospital discharge rate, which was improved from 5 to 7%, was not sufficient to show a significant result despite almost 3000 randomized patients. However, a new approach to evaluate outcome was devised by connecting short- and long-term survival rates in a χ-square trend test. This analysis revealed a significant difference in favour of ACD-CPR.

The implementation and evaluation of prehospital resuscitation studies should be reviewed. Before evaluating a new method of resuscitation standardized education guidelines must be established. The new method should be the subject of a pilot study before the main investigation. Thus, application problems can be recognized early and resolved. Regular quality monitoring during the study is mandatory. Prior to the study, it should be decided, whether the objective is a significant result in respect of short- or long-term survival rates. The corresponding power calculation will then determine the number of patients required for a genuinely significant result. If the hospital discharge rate of neurologically intact patients is chosen, then very large numbers of patients are required, which can only be achieved in time-consuming and expensive large-scale, multicentre studies. If short-term survival factors, such as haemodynamic parameters or the hospital admission rates, are chosen as primary objective variables, then the required number of patients is substantially reduced. At present it remains controversial whether long-term survival rates, which are influenced by many factors not directly related to the resuscitation method, are a better method than the combination of haemodynamic values and short-term survival rates.

5. Conclusions

In spite of encouraging haemodynamic results, all but one study failed to show an increase in long-term survival rates (hospital discharge without neurological damage, 1-year survival) with an alternative method in a convincingly large group of patients. In this study ACD-CPR increased long-term survival compared to standard-CPR. The results from certain individual studies which showed a significant increase in short-term sur-

vival rate could not be reproduced in other trials. This may be attributed in part to insufficient superiority of the alternative methods, but also to logistic and statistical defects with the conduct of the studies and clear differences in the application quality within and between the individual study sites. Of all the alternative methods, ACD-CPR has undergone the most intensive study and can be especially recommended as an alternative to standard resuscitation for patients with asystole in centres with effective training where outcome quality is regularly verified and evaluated.

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