

Cardiorespiratory interactions and blood flow generation during cardiac arrest and other states of low blood flow

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Purpose of review

Recent advances in cardiopulmonary resuscitation have shed light on the importance of cardiorespiratory interactions during shock and cardiac arrest. This review focuses on recently published studies that evaluate factors that determine preload during chest compression, methods that can augment preload, and the detrimental effects of hyperventilation and interrupting chest compressions.

Recent findings

Refilling of the ventricles, so-called *ventricular preload*, is diminished during cardiovascular collapse and resuscitation from cardiac arrest. In light of the potential detrimental effects and challenges of large-volume fluid resuscitations, other methods have increasing importance. During cardiac arrest, active decompression of the chest and impedance of inspiratory airflow during the recoil of the chest work by increasing negative intrathoracic pressure and, hence, increase refilling of the ventricles and increase cardiac preload, with improvement in survival. Conversely, increased frequency of ventilation has detrimental effects on coronary perfusion pressure and survival rates in cardiac arrest and severe shock. Prolonged interruption of chest compressions for delivering single-rescuer ventilation or analyzing rhythm before shock delivery is associated with decreased survival rate.

Summary

Cardiorespiratory interactions are of profound importance in states of cardiovascular collapse in which increased negative intrathoracic pressure during decompression of the chest has a favorable effect and increased intrathoracic pressure with ventilation has a detrimental effect on survival rate.

Keywords

cardiopulmonary interactions, cardiopulmonary resuscitation, shock, survival, ventilatory rate

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Dr. Lurie is a coinventor of the inspiratory impedance threshold device and active compression/decompression cardiopulmonary resuscitation technology and founded a company, CPRx LLC, to develop this device. There are no other conflicts of interest.

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Abbreviations

AED automatic external defibrillator
CPR cardiopulmonary resuscitation

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Koenig [1] proposed using chest compression as therapy for cardiac arrest in 1884. Kouwenhoven *et al.* [2] reintroduced the method in 1960, and, since then, there has been worldwide application of chest compressions in cardiopulmonary resuscitation (CPR). Despite this long history, our understanding of how chest compressions during cardiac arrest generate forward blood flow remains incomplete and divided into two schools of thought: the cardiac pump theory and the thoracic pump theory. Initially, the cardiac pump theory predominated. It was thought that pressing the heart between the sternum and spine generated the force to propel the blood from the ventricles to the lungs and systemic circulation, whereas recoiling of the chest promoted flow into the ventricles. It was not until 1976, when Criley *et al.* [3] described “cough resuscitation,” that the theory of a thoracic pump mechanism emerged. Based on the thoracic pump theory, the heart was thought to function more as a passive conduit, while during each chest compression, transmission of blood from the lungs to the systemic circulation occurred because of increased pressure in the intrathoracic arteries. The work of Weisfeldt and Halperin [4] further supported this hypothesis. Echocardiographic observations [5,6] have shown that both the cardiac and thoracic pump mechanisms are operative, but it is still unclear what determines which mechanism predominates. By contrast, it is during the decompression phase that venous blood flow returns to the heart secondary to differences between the extrathoracic and intrathoracic veins. As pressures decrease in the thorax relative to the extrathoracic vasculature, blood moves back to the right heart via the vena cava and, to a lesser extent, back to the left heart via the aorta. In reality, both the thoracic pump and cardiac pump mechanisms play an important role at different times after cardiac arrest.

Factors that might affect the relative roles of the cardiac and thoracic pumps include the time between arrest and CPR, venous return, total body volume status, cardiac chamber blood volume, cardiac valve integrity, vascular compliance, chest compression rate and depth, ability of the chest wall to recoil fully, duration of compression in relation to decompression, chest wall elasticity, airway pressure, ventilation rate, body habitus, hypoxia, hypercarbia, vasoactive medications, and presenting cardiac rhythm. The amount of blood flow to the heart at any given time may be the most important determinant of survival. Indeed, the amount of blood flow that returns to

the heart has recently emerged as a critical determinant of CPR efficacy and survival after cardiac arrest [7,8]. This review focuses on recently published studies that evaluate blood flow during chest compression, current concepts on the factors that determine preload during chest compression, methods that can augment preload, and the detrimental effects caused by interrupting chest compressions and hyperventilation.

Determinants of preload during cardiopulmonary resuscitation

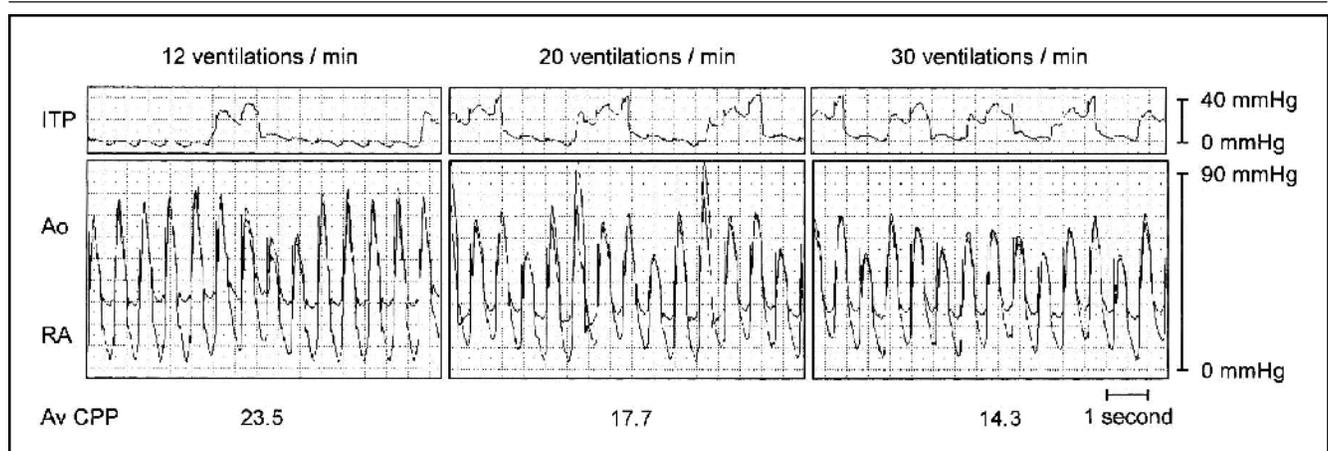
To maintain forward blood flow in a closed circuit such as the cardiovascular system, the fluid volume moving out of the heart must be matched by an equal return of volume into the heart. Refilling of the cardiac ventricles is diminished during cardiac arrest and cardiovascular collapse. Determinants of venous return or right ventricular preload during CPR for the treatment of cardiac arrest include intravascular volume, venous tone, microcirculatory perfusion, circulating neurohormones including catecholamine and vasopressin, recoil of the chest, and fluctuations in intrathoracic pressure. Preload of the left ventricle is influenced by similar factors as well as resistance to blood flow through the pulmonary vasculature, the integrity of the vasculature in the lungs, airway pressure, hypoxia, and hypercarbia. The multitude of interactions of each of these factors makes the study of blood flow during CPR extremely complex.

Recently, there has been a resurgence of interest in the importance of increasing negative intrathoracic pressure during the decompression phase of CPR. The idea was first reintroduced by a report of a successful resuscitation with a hand-held suction device applied to the chest of a family member in cardiac arrest [9]. This concept

inspired the development of an active compression/decompression CPR device [10,11] and resulted in a number of investigations on the subject [12,13]. The relevance of further increasing venous return by negative intrathoracic pressure was highlighted by the introduction of the concept of impeding inflow of air into the chest during recoil of the chest [14]. Additional studies in animals and humans have demonstrated that survival rates can be substantially increased by combining active compression/decompression CPR with an inspiratory impedance threshold device [8,14–16]. More recently, the potential benefit of this new concept has led to the recognition that an inspiratory impedance device may be of clinical utility as a cardiac preload device in a wide range of disease states, from hemorrhagic shock to vasovagal syncope [12]. Recent studies in hemorrhagic shock, in which application of the impedance threshold device produces improved cardiac output, blood pressure, and survival rates in animals, also suggest that this device may be particularly useful when intravenous fluids are not immediately available [17,18].

The rate and duration of each ventilation play a critical role in the amount of venous return to the heart during CPR. Increased ventilation rates affect return of the blood to the heart during CPR, resulting in reduced aortic blood pressure and coronary perfusion pressure (Fig. 1) [19]. High ventilation rates also significantly lower coronary perfusion pressure during a low-flow state induced by hemorrhage [20]. The faster the ventilation rate is, the more positive the intrathoracic pressure is per unit of time. This prevents effective venous blood flow back to the heart during CPR and in states of cardiovascular collapse. Contrary to the popular practice, ventila-

Figure 1.



In a porcine model of cardiac arrest, after 6 minutes of ventricular fibrillation, standard cardiopulmonary resuscitation was performed with an automated device (CPR Controller, Ambu International, Linthicum, MD) at a rate of 100 compressions per minute. This representative experiment demonstrates that coronary perfusion pressure and systolic blood pressure were significantly lower with higher compression ventilation ratios [19]. CPP is defined as aortic pressure minus right atrial pressure during decompressive phase. Ao, aortic blood pressure; Av CPP, average coronary perfusion pressure (mm Hg); ITP, intrathoracic pressure; RA, right atrial pressure.

tion rates must be decreased, not increased, in the setting of cardiac arrest and hypovolemic shock.

Two recent studies examined how different ventilation methods affect survival [21•,22•]. Kern *et al.* [21•] conducted a study of 20 pigs after prolonged cardiac arrest of 10 minutes in which they assessed how four different methods of ventilation affected phased chest and abdominal compression/decompression resuscitation, a method designed to augment preload during CPR. Ventilation methods were asynchronous ventilation at a 5:1 ratio, synchronous ventilation at rate of 15:2 or 5:1, and passive “ventilation” alone. Asynchronous ventilation resulted in lower coronary perfusion pressure and a lower 24-hour survival rate than other methods of ventilation [21•]. Asynchronous intermittent positive pressure ventilation was also found to have a detrimental effect with lower aortic blood pressure and a lower survival rate in an animal study by Kleinsasser *et al.* [22•]. This CPR study compared asynchronous intermittent positive pressure ventilation with either continuous positive airway pressure ventilation alone or continuous positive airway pressure with decompression-triggered, positive-pressure ventilation. In the study, CPR was started immediately after induction of ventricular fibrillation because of low coronary perfusion pressures. With decompression-triggered, positive-pressure ventilation and a chest compression rate of 80 per minute, the tidal volume was low, but the ventilation rate was high (73 ± 16 breaths per minute). Of interest is that decompression-triggered, positive-pressure ventilation uses a thorax pump mechanism to generate forward blood flow during CPR. The study results were compromised by use of high, continuous, positive airway pressure (12 cm H₂O) and low coronary perfusion pressures. The same level of positive airway pressure was found to decrease preload in a dog study by Fewell *et al.* [23]. It remains unknown whether this approach has any clinical value because continuous positive airway pressure inhibits venous return to the heart during the early decompression phase of CPR, thereby reducing overall CPR efficacy.

Augmentation of preload

With the exception of administration of exogenous fluid replacement or placement into the Trendelenburg position, there are limited ways to enhance blood flow back to the heart during CPR. Use of intravenous fluids during CPR does not play a large role in the current American Heart Association guidelines [24]. That reflects observations from animal studies showing how infusion of large volumes of blood or isotonic solutions during CPR decrease myocardial perfusion pressure and blood flow [25–27]. However, based on the observation of a plasma shift from the intra- to the extravascular compartment leading to intravascular hypovolemia and the hemoconcentration phenomenon during cardiac arrest [28,29], Fischer *et al.* [30•] recently conducted a study on the

effect of low-volume hypertonic resuscitation on blood flow during CPR. Hypertonic saline (7.2% NaCl) was applied at the start of open chest cardiac massage in a porcine model of prolonged cardiac arrest (10 minutes). Infusion of 2 mL/kg in 10 minutes or 4 mL/kg in 20 minutes enhanced myocardial blood flow and cardiac index and significantly increased resuscitation success and survival rates [30•]. Hypertonic saline has been shown to be deleterious in hearts with impaired contractile function caused by ischemia [31,32]. However, in this study using normal hearts, there was no increase in central venous or diastolic left ventricular pressure, which would have indicated reduced right or left ventricular contractility.

Augmentation of preload during CPR with different devices may not carry the same long-term side effects as medications or intravenous fluids. For example, an impedance threshold device has been found to increase preload and has been used in animal models and human subjects in cardiac arrest [8,14–16,33•,34,35••,36••]. Each time the chest recoils during the performance of standard CPR, the impedance device transiently blocks air from entering the lungs, generating increased vacuum within the chest that sucks blood into the heart. The device is designed to prevent inspiratory gas exchange only until a cracking pressure is achieved but does not affect the expiratory phase. In addition, active rescuer ventilation remains unimpaired by this device. This cracking pressure can be altered during the manufacturing process, and the cracking pressure has been tested from 15 to 24 cm H₂O in CPR studies. This cracking pressure could increase substantially the work of breathing in a spontaneously breathing subject, and it is therefore recommended that the device be removed as soon as subjects start breathing spontaneously. In an animal model of cardiac arrest, using of the impedance threshold device during performance of standard CPR after 6 minutes of cardiac arrest resulted in a significant increase in neurologically intact 24-hour survival rates compared with animals treated with a sham device [35••].

Little experience exists with use of an impedance threshold device in the pediatric model of cardiac arrest. Until recently, it had only been studied in adult animals models and adult human subjects. In a piglet model (8–12 kg), the combination of active compression/decompression with the inspiratory threshold valve during CPR was found to significantly increase both coronary perfusion pressure and vital organ blood flow after prolonged (10 minutes) ventricular fibrillation [36••].

In light of the observation that both standard CPR and active compression/decompression CPR can cause fatigue, frequent rotation of rescuers is advised. Recently, an automatic mechanical compression and active decom-

pression device was described [37•]. The investigators reported that the automated device improved the efficacy of CPR in an animal model of prolonged cardiac arrest. The device is powered by compressed gas.

Finally, abdominal compression during CPR in the form of interposed abdominal counterpulsations can also increase the venous return to the heart [21•]. Although the timing of the alternating compression of the chest, decompression of the chest, and compression and release of the abdomen is complex, there is no doubt that venous blood flow back to the heart can be enhanced by abdominal counterpulsation. With this approach, it is critical to allow a sufficient amount of time after the chest has recoiled and before the abdomen is compressed to facilitate improved coronary artery perfusion [38]. This technique has recently been advanced further with a device called the LifeStick (Datascope, Fairfield, NJ) [21•]. It helps to perform both active compression and decompression of both the chest and abdomen, resulting in increased coronary perfusion pressure [39]. A recent small study in patients failed to demonstrate a difference in resuscitation rates with the LifeStick compared with standard CPR [40]. Training may have been an important issue in that study.

Interrupted chest compressions

Another critical variable affecting cardiopulmonary function during CPR relates to how ventilation and compression are delivered in the field. A recent and concerning observation by Assar *et al.* [41] indicated that during CPR, there were, on average, 16-second pauses in chest compressions with two ventilations during standard 15:2 single-rescuer CPR. The study was designed to evaluate different teaching methods of CPR. In those who performed standard CPR, there were, on average, only 39 actual chest compressions delivered per minute because of frequent interruptions for ventilation. The group that performed continuous chest compressions with a short resting period every 50 compressions averaged 84 actual compressions per minute.

Based on these results, Kern *et al.* [42••] simulated these observations in an animal study of single-rescuer standard CPR versus continuous compression CPR. In their animal study, there was ventricular fibrillation for 3 minutes followed by prolonged CPR. Defibrillation was attempted after 15 minutes of cardiac arrest. Survival rates were markedly improved over 24 hours in pigs with uninterrupted CPR versus CPR with a 15:2 compression to ventilation ratio with a 16-second pause to simulate the delivery of the ventilation duration observed by Assar *et al.* [41]. In further support of the importance of performing continuous and uninterrupted chest compression, a recent study compared the effect of teaching by emergency medical services discharge the laypersons calling 911 either chest compressions alone versus both

mouth-to-mouth ventilation and chest compression. Chest compressions alone, without ventilations during lay bystander CPR were no worse than standard CPR [43]. Although controversial because there is concern related to adverse outcomes resulting from lower oxygen concentrations found with continuous chest compressions without rescue breathing [44], it is clear that interruptions in chest compressions for frequent ventilation will decrease coronary perfusion pressure [45]. It is also clear that chest compressions alone are better than or at least equivalent to chest compressions plus mouth-to-mouth ventilation in the first few minutes after cardiac arrest if professional rescuers are not available [43].

Using mathematical analysis, Monte Carlo simulations, and principles of classical physiology, Babbs and Kern [46••] found that current American Heart Association guidelines overestimate the need for ventilation during standard CPR by two- to fourfold. Compared with a 5:1 ratio, there was greater calculated delivery of oxygen to the body with a 30:2 or 60:2 ratio in which slightly decreased arterial oxygen content was overcome by increased blood flow. They concluded that blood flow and oxygen delivery to the periphery could be improved by decreasing interruptions of chest compression for unnecessary ventilations.

For similar mechanistic reasons, interruption of CPR when using an automatic external defibrillator (AED) can also be harmful because there is no perfusion while the AEDs are “thinking” and charging before delivering a shock. Cobb *et al.* [47••] showed that after full implementation of AEDs in Seattle, survival rates did not demonstrate the anticipated increase in survival but rather the inverse. This could be explained by a delay in implementing CPR while the AED is set up or that with AED use there is a prolonged period of interrupted chest compressions while the AED is analyzing the rhythm. CPR before the first shock has been found to increase the likelihood of survival [47••,48]. Interruption of chest compressions for an AED required rhythm analyses ranging from 10 to 19.5 seconds [49••]. This observation prompted an animal study by Yu *et al.* [49••], in which they interrupted CPR for 3, 10, 15, or 20 seconds before defibrillation. The study showed that interruptions of chest compressions that exceeded 3 seconds compromised the survival from CPR: all of the animals with 3 seconds of interruption survived, whereas none of those with 20 seconds of interruption survived. In this study, additional vasopressor medications were not used to simulate the practice of emergency technicians, without advanced life support, in the field [49••].

Conclusions

Recent advances in CPR have led to an emphasis on early defibrillation. However, despite the widespread use of early defibrillation, survival rates from cardiac ar-

rest remain poor. Recent studies on out-of-hospital arrest emphasize the need to revisit the basic critical elements of CPR. Improving the quality of CPR and application of CPR before defibrillation improves resuscitability. In a low-flow state, the generation of blood pressure by “priming the pump” is heavily dependent on venous return and blood flow through the lungs. Any interruption of this process will inevitably result in prolonged hypoperfusion and delayed return to normal rhythm.

Very few methods enhance blood flow back to the heart during cardiac arrest. Active compression/decompression during CPR has been found to increase blood flow during CPR. Another device, the LifeStick combines chest compressions with active decompression to the resting position of the chest wall. A third device, an inspiratory impedance device, increases blood flow during cardiopulmonary resuscitation by increasing negative intrathoracic pressure during recoil of the chest in CPR, thereby drawing more blood back to the right heart. Its effect is augmented with compression/decompression CPR, and it results in improved survival rates in patients after cardiac arrest.

Finally, it has become increasingly clear that future methods need to be developed to optimize tissue oxygenation while simultaneously minimizing the increase in intrathoracic pressure with each positive pressure ventilation. Although ventilation is critical during cardiac arrest, recent clinical and animal data have demonstrated that currently practiced ventilation rates are far in excess of what is needed for adequate tissue oxygenation. Moreover, when chest compressions are interrupted to deliver positive pressure ventilation, cardiac perfusion and subsequently survival rates decrease. The ideal number of breaths per minute, the duration and amplitude of the increase in intrathoracic pressure with each positive pressure ventilation, and the potential benefit of periodic high-frequency ventilation (500–1000 Hz) remain important areas of research. The development of new ventilation strategies during states of low blood flow will be critical for optimizing cardiopulmonary interactions and ultimately tissue perfusion for the patient in cardiac arrest or severe hypotension. Although important steps toward understanding the interactions between respiration and cardiac perfusion have already been taken, further research is essential to optimize these interactions during treatment of cardiovascular collapse.

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