Bringing Back the Nearly Dead

The Hope and the Challenge

By Keith Lurie, M.D.

ABSTRACT

Despite widespread use of cardiopulmonary resuscitation, sudden cardiac arrest outside of a hospital setting results in death most of the time. Hoping to improve resuscitation outcomes, University of Minnesota researchers have focused their efforts on understanding cardiopulmonary physiology and improving resuscitation technologies and procedures. This article describes new technologies, designed to be used in conjunction with standard CPR, that promote recovery from cardiac arrest. Active compression-decompression CPR, which involves use of a suction cup device to draw more blood into the heart and air into the lungs, has been shown to double 1-year survival rates. The inspiratory impedance threshold valve (ITV), when attached to an endotracheal tube or face mask, has been shown to increase cardiopulmonary circulation. An electrical stimulator device for the phrenic nerve, designed to evoke a gasp reflex, is under development. This device, when used in conjunction with the ITV, is thought to increase airflow into the lungs and blood flow into the heart, and may be beneficial for patients in hemorrhagic or heat shock as well as those in cardiac arrest.

Introduction

Every day more than 1,000 people die outside of the hospital from sudden cardiac arrest in the United States. Despite cardiopulmonary resuscitation (CPR), fewer than 5% of these unfortunate patients actually survive nationwide. In Minnesota, our results are slightly better—about 10% of all patients with an out-of-hospital cardiac arrest survive to eventually walk out of the hospital. Indeed, this is a national medical disaster in need of urgent care.

Why do so many people die despite receiving CPR from the 911 response teams? The reasons for this dismal track record can be summarized simply: Help comes too late, current CPR techniques are not very effective, and many of these patients have such severe disease that nothing can help.

Resuscitating CPR

Inspired by a patient who did survive, actually after three separate cardiac arrests on different days, because his family used a common household plunger to resuscitate him, investigators at the University of Minnesota have been finding new ways to resuscitate patients for more than a decade.[1] Not only did this humorous anecdote make it into one of Jay Leno's monologues—Why do plumbers charge as much as cardiologists?—it also inspired a breakthrough in life-saving technologies, not only for patients in cardiac arrest but also for those in shock secondary to hemorrhage and heat stroke. The new therapies, each at a different stage of development, have been recently shown to increase survival rates after cardiac arrest.[2-9] Some of these advances are now recommended in the new American Heart Association Guidelines for CPR.[10]

Although rapid access to the patient in cardiac arrest remains a challenge, the index case helped us focus on ways to improve the efficiency of CPR itself. Standard manual CPR provides only 10 to 20% of the normal blood flow to the heart and about 25% of normal blood flow to the brain. By lifting the chest after each chest compression with a suction cup device, more air and blood is drawn into the lungs with each active compression-decompression cycle, which improves overall CPR efficiency. In recent studies in France, use of a hand-held suction cup device applied to the chest of patients in cardiac arrest has been shown to double 1-year survival rates, and this has led to its widespread use by emergency rescue personnel.[2] This new technique is called active compression-decompression or ACD CPR. However, even with this new approach, most patients in cardiac arrest still die.

Keith Lurie is co-inventor of the impedance threshold valve and the active compression-decompression CPR devices, and founded CPRx LLC to develop the impedance threshold valve described in this article.

Figure 1

Impedance Threshold Valve

1a. This impedance threshold valve, the ResQPod, is used to increase circulation during cardiac arrest and other states of low blood pressure. It works by increasing venous return to the heart. It can be attached to an endotracheal tube or a face mask, as shown in 1b.

1a

1b

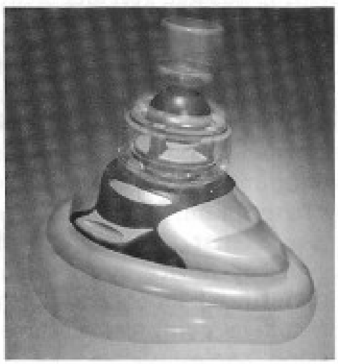
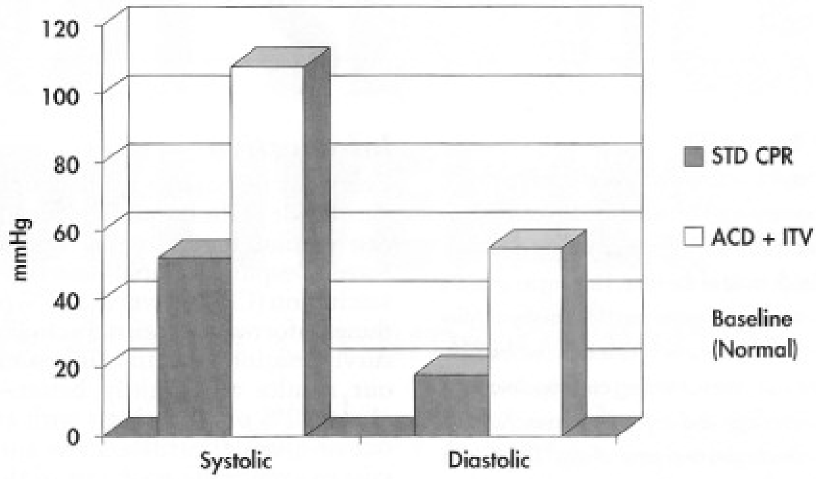


Figure 2

Blood Pressure in Cardiac Arrest Patients

Blood pressure was measured in a group of patients in cardiac arrest undergoing standard manual CPR and compared with those who received active compression decompression (ACD) CPR in combination with an impedance threshold valve (ITV).[5]



Further Research at the University of Minnesota

Although the ACD device, by itself, creates a vacuum within the thorax with each chest wall decompression, much of the potential hemodynamic benefit of this vacuum is lost by the influx of inspiratory gases. Observing this, investigators at the university developed an inspiratory impedance threshold valve (ITV) in 1995 to block this influx of inspiratory gases during chest wall decompression, thereby augmenting the amplitude and duration of the negative intrathoracic pressure.[3,4] This creates a larger vacuum within the thorax, forcing more venous blood back into the heart with each compression-decompression cycle, resulting in an increase in cardiopulmonary circulation.

The ITV is a small (35 mL) disposable plastic valve that is attached to the endotracheal tube or facemask (see Figure 1). It works by allowing the rescuer to freely ventilate the patient but impedes inspiratory airflow selectively during the decompression phase of CPR, when not actively ventilating the patient. This creates a small vacuum within the chest to further enhance venous return back to the heart.

Animal and clinical studies have now demonstrated that the combination of ACD CPR and an impedance valve improves coronary perfusion pressures and results in a greater-than-3-fold increase in blood flow to the heart and brain when compared with standard CPR alone.[3-5] The blood pressure in patients in cardiac arrest who receive this new method of CPR is nearly normal (see Figure 2).[5] Two clinical trials from Europe evaluating the ITV in more than 650 patients with out-of-hospital cardiac arrest will be published later this year. One of these studies in France showed that the use of the ITV together with ACD CPR results in a 50% increase in 24-hour survival rates.[11] The neurological function of the survivors was significantly improved compared with those who received ACD CPR alone. In a second study from Germany, unpublished at present, comparing standard manual CPR with the combination of ACD CPR and the impedance valve, 24-hour survival rates increased by 100% in patients who had a witnessed cardiac arrest.[12] Survivors in that study also had a marked improvement in their brain function at the time of hospital discharge. In the subset of patients with the greatest likelihood for survival, those with a witnessed cardiac arrest in ventricular fibrillation, there was a 55% hospital discharge rate for patients treated with the new technology. Taken together, these exciting results support the

Figure 3

Echocardiogram of Animal in Hemorrhagic Shock

This is a m-mode echocardiogram from an animal in hemorrhagic shock. When phrenic nerve stimulation is used in conjunction with an inspiratory impedance valve to induce a gasp, there is a large increase in right ventricular volume (black space), indicative of enhanced venous return.

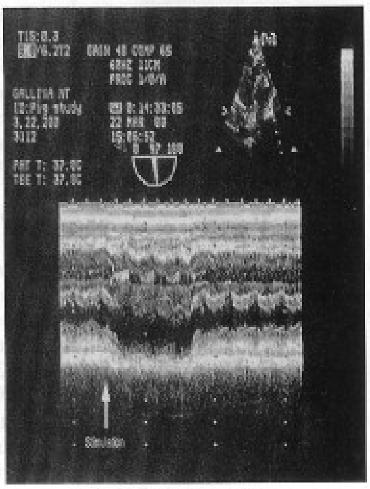
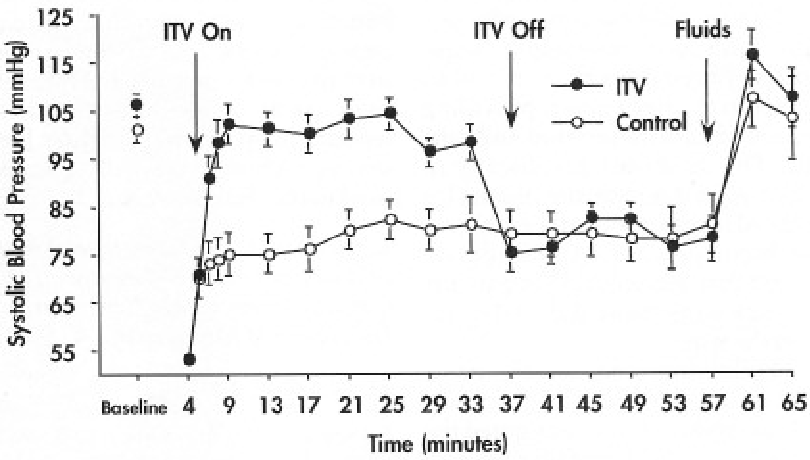


Figure 4

Blood Pressure of Animals in Hemorrhagic Shock

During shock from blood loss the use of an inspiratory impedance threshold valve (ITV), set to open at 12 cm H_2O, results in a rapid and sustained rise in blood pressure for at least 30 minutes. At that time the valve is removed, and pressures fall to baseline values until fluid resuscitation is available.



more generalized use of this technology.

Most recently, animal studies have also shown that blood flow to the heart and brain is doubled by the addition of the ITV during performance of standard CPR. This also significantly increases survival rates and brain function after survival.[6,7] A large clinical trial is underway in Milwaukee, Wisconsin, to test this new technology with standard manual CPR. If the results are promising, then the ITV may become part of the standard approach to CPR used by both professional and lay rescue personnel (more than 10 million people are taught this approach each year).

The Last Gasp

Previous investigators have observed that patients in cardiac arrest who are gasping have a better chance for survival.[13] This intriguing observation suggests that the body may, under dire circumstances, attempt to draw more air into the lungs and more blood back into the heart with agonal breathing as part of the last gasp. Building upon the lessons of ACD CPR and the impedance valve, we developed an electrical stimulator device to induce a gasp reflex.[7,8] It works by electrically stimulating the phrenic nerve with transcutaneous electrodes. In conjunction with the ITV, application of the phrenic nerve stimulator results in a vacuum within the thorax, in a manner similar to that observed during ACD CPR with the impedance valve. It has been a challenge to demonstrate conclusively that this approach will work during cardiac arrest probably because the high metabolic requirements of the diaphragm associated with repetitive diaphragmatic stimulation during CPR. However, the phrenic nerve stimulator may be a useful device for other states of low blood pressure. Specifically, use of the phrenic nerve stimulator combined with the ITV is effective in the treatment of hemorrhagic shock.[7,8] This can be seen graphically by m-mode echocardiography in an animal model of shock (see Figure 3). Each time the stimulation pulse is applied, it results in a bolus of blood delivered back to the right heart. In effect, the combination of the phrenic nerve stimulator and ITV provides a preload to the heart, priming the pump for the next contraction.

Shock and a Vikings Football Player

The concept of creating a vacuum in the chest when the pressure within the thorax is below atmospheric pressure can also help patients with hypotension who are not in cardiac arrest. Building upon the idea of creating a vacuum in the chest by diaphragmatic stimulation, our most recent studies have focused on the potential role of the impedance valve in models of shock in which the patient is spontaneously breathing. With both phrenic nerve stimulation and with spontaneously breathing animals, use of the impedance valve appears to buy time until more definitive care is available. The first studies were performed in animals in hemorrhagic shock.[14] In these studies, animals are anesthetized but allowed to breathe spontaneously. After hemorrhage, inspiration through an impedance valve, set to open at a low resistance of around 12 cm H_2O, results in a small but critical vacuum within the heart with each spontaneous inspiration. This causes more blood to return to the right heart, providing increased cardiac preload and output. This is shown graphically in Figure 4. In this case, use of the ITV resulted in restoration of nearly normal blood pressures. Clinically, we believe that this will help in patients in shock while more definitive care is on the way.

Following the death of a Vikings football player secondary to heat stroke, we also evaluated the potential for the impedance valve to restore blood pressure after heat shock.[15] We hypothesized that augmentation of venous return may be particularly helpful in the setting of profound vasodilation. Indeed, use of the ITV had a similar effect during heat shock as we observed during hemorrhagic shock. That is, with inspiration against a small resistance there was a rapid and sustained increase in blood pressure for a sufficient period of time to enable us to cool the animals in shock. We are now collaborating with U.S. Army scientists to determine if this overall approach will be useful for treating shock secondary to excessive hemorrhage and heat in humans.

Pathway to the Patient

Although the physiology and technology underlying the use of the impedance valve may seem simple and intuitive, the complex cardiopulmonary interactions that lead to forward blood flow within the cardiovascular system in states of very low blood pressure remain fertile grounds for investigation and discovery. We still have a lot to learn about how the body responds to severe stress associated with shock and cardiac arrest. Despite the progress, the pathway from the laboratory to the bedside, or in our case, the roadside, is filled with pitfalls and potholes. We are optimistic that ongoing collaboration with co-investigators in U.S. and European test sites, as well as collaboration with NASA and U.S. Army researchers, will demonstrate further benefits of this technology in patients in shock and cardiac arrest over the next 1 to 2 years. Although there are many regulatory hurdles, we remain optimistic that these lifesaving technologies will soon be used in the clinical arena.

Keith Lurie is an associate professor of medicine and co-director of the Cardiac Arrhythmia Center at the University of Minnesota.

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