

Augmentation of ventricular preload during treatment of cardiovascular collapse and cardiac arrest

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Despite aggressive measures for the treatment of cardiovascular collapse and cardiac arrest, the hypotension associated with these malignant processes usually leads to profound vital-organ ischemia and death. A fundamental therapeutic challenge of such life-threatening processes is the restoration of adequate blood flow to the heart and the brain. However, to maintain adequate forward blood flow out of the heart, venous blood return must be drawn back into the heart. With the exception of administration of exogenous fluid replacement, there are limited ways to enhance blood flow back to the heart during prolonged hypotension. This article describes the potential value of a new impedance threshold valve for the treatment of cardiac arrest and

hypotension. The valve was designed to create a vacuum within the thorax during the decompression phase of cardiopulmonary resuscitation or during inhalation. By transiently blocking inspiratory gas exchange during the decompression phase of cardiopulmonary resuscitation, after phrenic nerve-stimulated gasping, or during spontaneous ventilation, the impedance-valve concept may have clinical value in the treatment of patients in cardiac arrest, hemorrhagic shock, and cardiovascular collapse secondary to a number of life-threatening clinical processes. (*Crit Care Med* 2002; 30[Suppl.]:S162–S165)

KEY WORDS: cardiac arrest; shock; hypotension; impedance threshold valve; ventricular fibrillation; hemorrhage

An essential element for maintenance of adequate forward blood flow out of the heart is sufficient venous return back to the heart with each cardiac cycle. As simple as this concept may seem, it is the distinct lack of venous return to the heart during states of profound hypotension that often leads to the downward spiral of ischemia, acidosis, hypoxemia, and ultimately, death. Thus, to sustain effective blood flow through a closed-loop system such as the cardiovascular tree, during each cardiac cycle, the fluid volume moving forward out of the pump must be matched by an equal volume of blood from the rest of the body moving back into the pump. Refilling of the ventricles, the so-called ventricular preload, is diminished during cardiovascular collapse and cardiac arrest. Although fluid replacement, positioning in the Trendelen-

burg position, or vasopressor administration can be life-saving measures, such measures are often inadequate or initiated too late.

In an effort to enhance ventricular preload during cardiac arrest and cardiovascular collapse, an inspiratory impedance threshold valve was developed to intermittently decrease intrathoracic pressures to drive venous blood back into the right side of the heart (1–4). During the treatment of cardiac arrest, the impedance valve causes a decrease in intrathoracic pressure within the thorax each time the chest wall recoils during the decompression phase of cardiopulmonary resuscitation (CPR). By selectively blocking inspiratory gas exchange when not actively ventilating the patient, the impedance valve causes a vacuum within the chest, which draws blood back into the heart, augmenting ventricular filling for the next compression phase. In animals and patients in cardiac arrest, use of the inspiratory impedance valve has resulted in improved vital organ perfusion and increased survival rates (5, 6).

A similar mechanism may also be useful for the treatment of cardiovascular collapse secondary to severe hemorrhage. In apneic animals in shock, phrenic nerve stimulation can be used to induce a gasping reflex electrically (1, 7). This causes the animal to inspire. When phrenic nerve stimulation is used with an inspira-

tory impedance valve, the combination results in increased ventricular preload and survival (7, 8). In a similar manner, in spontaneously breathing animals in hemorrhagic shock, inspiration through the impedance valve has an instantaneous and marked effect on ventricular preload and treatment of severe hypotension. Intrathoracic pressures decrease with each inspiration and systolic and diastolic pressures increase (K Lurie et al., unpublished observations).

Experimental support for the use of the impedance threshold valve for the treatment of cardiovascular collapse and cardiac arrest is provided below. At present, there has only been a limited amount of clinical experience with this device (P Plaisance et al., unpublished observations) (6, 9). If further studies confirm this concept, it is possible that variable degrees of inspiratory impedance for both apneic and spontaneously ventilating patients may be of value for the treatment of a wide range of physiologic processes in which ventricular preload is insufficient, including cardiac arrest, hemorrhagic shock, cardiovascular collapse secondary to hyperthermia, shock secondary to drowning, right ventricular infarction, vasovagal syncope, and shock secondary to high-gravitation forces. Moreover, the augmentation of forward blood flow afforded by the use of the valve may enhance the circulation of life-

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Dr. Lurie is the co-inventor of an impedance threshold valve that is described in this paper. He will benefit from the sale of this device.

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saving adjunctive drug therapies (10). Thus, the impedance valve may enhance drug efficacy and potentially decrease drug toxicity, especially in the setting of cardiac arrest.

USE OF THE IMPEDANCE VALVE FOR CARDIAC ARREST

The inspiratory impedance threshold valve has been used in animal models and in human patients in cardiac arrest (1–7, 9, 10). Each time the chest recoils during the performance of standard CPR, the impedance valve transiently blocks respiratory gases from entering the lungs, generating a small vacuum within the chest that sucks blood back into the right side of the heart. The valve is designed to prevent inspiratory gas exchange until a cracking pressure is achieved. This cracking pressure can be altered during the manufacturing process. For the treatment of cardiac arrest, the safe valve cracking pressure on the impedance valve has been set to 21 cm H₂O; at that point, respiratory gases can pass through the valve into the animal or patient. Thus, should a patient begin to breathe spontaneously, ventilation through the valve would be possible before the removal of the valve from the respiratory circuit by the rescuer. It is important to note that the patient must be ventilated when using the impedance valve, as with standard CPR, until spontaneous breathing has been restored. Then the valve must be removed from the ventilation circuit.

In pigs, use of the valve resulted in a 40% increase in coronary perfusion pressure during standard CPR, calculated as the mathematical difference between the diastolic aortic and right atrial pressures (4). However, such measurements seem to underestimate the benefit of the valve. By using radiolabeled microspheres to measure vital organ perfusion, myocardial perfusion was increased by 100% and cerebral perfusion was increased by 80% in the same experiment (4). As the true test for any CPR adjunctive device is to demonstrate a survival benefit, the impedance valve was tested in the same porcine model of cardiac arrest to determine whether it could improve survival (5). After 6 mins of ventricular fibrillation and 6 mins of standard CPR, animals received three direct-current shocks. When this therapy was unsuccessful, animals that remained in cardiac arrest received

epinephrine (0.045 mg/kg), 90 additional seconds of CPR, and three more shocks. Survival rates at 24 hrs were 55% in the sham-valve group (n = 20) vs. 85% in the active-valve group (n = 20; $p < .05$). Only 1 of 11 animals in the sham-valve group had completely normal neurologic function compared with 12 of 17 survivors in the active valve group.

The impedance valve has also been evaluated during the performance of active compression-decompression CPR in an animal model (2). Using an automated device to actively compress and then decompress the chest with a suction cup attached to the anterior chest wall, the combination of active decompression and the impedance valve resulted in a four-fold increase in myocardial perfusion and a three-fold increase in cerebral perfusion compared with standard CPR alone. The combination of active compression and decompression with the impedance valve lowered decompression phase intrathoracic pressures, improved CPR efficiency, improved survival rates, and lowered defibrillation thresholds. A recent study has demonstrated the combination of active compression-decompression CPR with the impedance valve also enhanced vasopressor therapy efficacy during hypothermic cardiac arrest in pigs (11).

Experience in humans has been more limited, but it too has been supportive of the potential benefits of the impedance valve during cardiac arrest. In patients in prolonged cardiac arrest, the addition of the impedance valve to the care of patients undergoing active compression-decompression CPR resulted in higher end-tidal CO₂ levels and nearly normal blood pressures (mean, 110/55 mm Hg) compared with active compression-decompression CPR alone (mean, 90/40 mm Hg) (6). A second study demonstrated that the vacuum effect of the impedance valve was observed when using either a face mask or an endotracheal tube for ventilation (P Plaisance et al., unpublished observations). In patients with out-of-hospital cardiac arrest, pressures during active compression and decompression within the trachea were lower each time an active impedance valve was compared with a sham valve (Fig. 1). Finally, a more recent study compared the 24-hr survival rates for patients who received a sham valve vs. an active valve for treatment of out-of-hospital cardiac arrest (9). In this study, all patients received active compression-decompression CPR. Either an active (n

= 200) or sham (n = 200) valve was added to the patients' endotracheal tube in a blinded, prospective, randomized manner when advanced life support arrived. Twenty-four-hour survival, the primary end point, increased by 50% in the active impedance-valve group. Hospital discharge rates and neurologic function also trended higher with the active impedance valve.

An ongoing study in Mainz, Germany, comparing standard CPR vs. the combination of active compression-decompression CPR with the impedance valve will be finished by January 2002. The preliminary results from that study are similar to that which has been observed in the animal models and in other human studies on the impedance valve described above. Taken together, these data add further support to the critical importance of maintaining ventricular preload during the treatment of cardiac arrest.

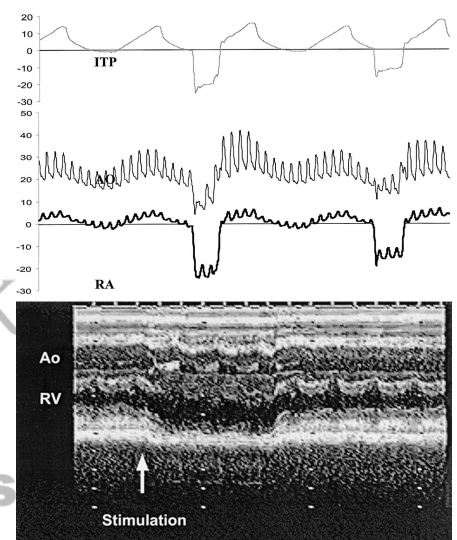


Figure 1. Top, representative tracings of intrathoracic pressure (ITP), right atrial pressure (RA), and systolic aortic pressure (AO) during periodic phrenic nerve stimulation combined with an impedance threshold valve in a porcine model of hemorrhagic shock. Animals were ventilated 12 times/min, and stimulation was performed after every other ventilation for 1 sec. Bottom, representative M-mode tracing made with a transesophageal echocardiograph before, during, and after phrenic nerve stimulation combined with an impedance threshold valve from the same representative experiment shown in the top panel. The M-mode vector transverses the right ventricle. The arrow indicates the point at which phrenic nerve stimulation was initiated. The large dark region that expanded during phrenic nerve stimulation is the right ventricle.

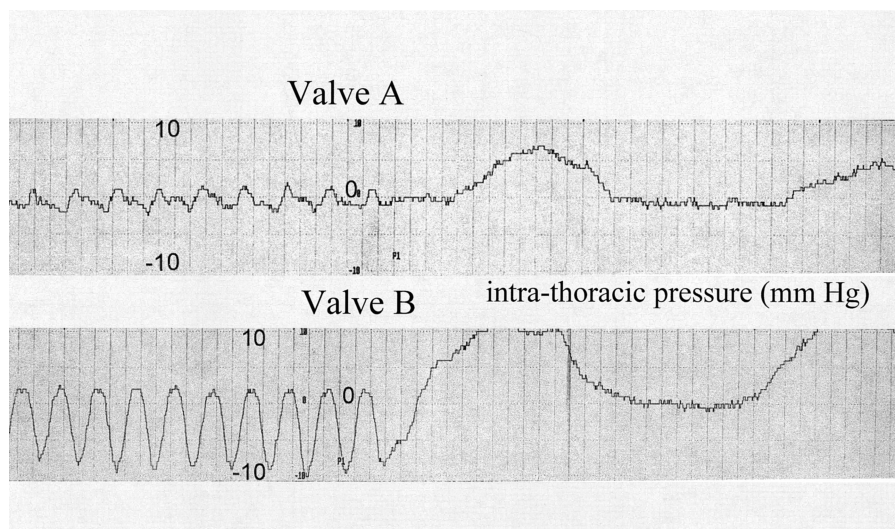


Figure 2. Representative tracing demonstrating the differences in intratracheal pressures recorded in a patient in cardiac arrest who was ventilated with a sham and then an active impedance threshold valve while undergoing bag-mask ventilation. The face mask was held in place by one rescuer while a second rescuer squeezed the ventilation bag. The patient received 15 active compressions and decompressions with an active compression-decompression cardiopulmonary-resuscitation device, followed by two ventilations delivered by the rescuer. In this example, *valve A* was a sham valve and *valve B* was an active valve.

Use of the Impedance Threshold Valve for Shock

Augmentation of venous return may also play an essential role in the treatment of other hypotensive emergencies, for example, shock secondary to hemorrhage, right ventricular infarction, hyperthermia, vasodepressor syncope, drowning, and during exposure to high-gravitation forces. In each of these cases, there may be inadequate blood flow back to the heart with each cardiac cycle. We have studied the potential value of the impedance threshold valve during electrically induced inspiration or gasping in animal models of hemorrhagic shock (7, 8). More recently, we have used the impedance valve in spontaneously breathing animals in hypotensive crises.

Phrenic nerve stimulation causes the diaphragms to contract. Using transcutaneous electrodes to stimulate the phrenic nerve, we evaluated the combination of the impedance valve with phrenic nerve stimulation in a porcine model of hemorrhagic shock (7, 8). With each stimulation, there was a marked decrease in intrathoracic pressure. This resulted in a profound increase in right ventricular volume; consistent with the hypothesis that ventricular preload could be enhanced with a decrease in intrathoracic pressure (Fig. 2). The increase in transvalvular flows and ventricular volumes

that was observed with each electrically-induced gasp also resulted in improved short-term survival after hemorrhagic shock when compared with controls. In that study, one of seven animals survived for 30 mins with hemorrhagic shock in the control group vs. six of seven in the group treated with the combination of periodic phrenic nerve stimulation (12 times/min) and the impedance valve. Without the impedance valve, the energy required to achieve a similar decrease in intrathoracic pressure was 50% higher and the vacuum effect was not as great. The concept of using a transcutaneous phrenic nerve stimulator with the impedance valve has only been tested, at this time, in animal models. Although muscle fatigue and issues related to high skin impedance remain potential barriers to further development, none appear insurmountable at this time. However, the results support the underlying premise that periodic decreases in intrathoracic pressures will enhance ventricular preload and improve hemodynamic stability during profound shock.

In addition to studying the potential benefits of an impedance valve during phrenic nerve-stimulated inspiration, recent studies have demonstrated that use of the impedance valve may have a marked effect on blood pressure and venular preload in spontaneously breath-

These observations suggest that decreasing phasic intrathoracic pressures by using an impedance threshold valve may help to pump blood back into the heart during cardiac arrest and shock secondary to multiple causes.

ing animals in hemorrhagic shock (K Lurie et al., unpublished observations). Using a similar porcine model of shock described above, animals anesthetized with propofol were allowed to breathe spontaneously while still receiving anesthesia. In the absence of ventilatory support, the anesthetized animals maintained normal blood gases. Once hypotension to 50 mm Hg was achieved by active hemorrhage, animals were randomized to either an active or sham impedance valve with a safety check-valve cracking pressure of 12 cm H₂O. The impedance valve opened once the intrathoracic pressure reached a level of -12 cm H₂O, allowing for spontaneous inspiration through the valve. Similar to the results with the electrically induced gasping described above, in spontaneously breathing animals in shock, placement of the impedance valve within the respiratory circuit resulted in an immediate and sustained rise in aortic systolic and diastolic pressures of greater than 30 mm Hg. After 30 mins, the impedance valve was removed and the blood pressures returned to the control values observed before the addition of the impedance valve. Similar observations have also been made in pigs in shock secondary to hyperthermia (K Lurie et al., unpublished observations).

CONCLUSIONS

Taken together, the observations described in this article suggest that decreasing phasic intrathoracic pressures by using an impedance threshold valve may help to pump blood back into the

heart during cardiac arrest and shock secondary to multiple causes. The impedance-valve concept requires a means to lower intrathoracic pressures while simultaneously allowing for adequate ventilation. The decrease in intrathoracic pressure can be accomplished by the natural recoil of the chest during standard CPR, the active recoil of the chest during active compression-decompression CPR, or by the activity of the diaphragms during spontaneous breathing or electrical stimulation of the diaphragms.

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