Optimizing Standard Cardiopulmonary Resuscitation With an Inspiratory Impedance Threshold Valve*

Keith G. Lurie, MD; Katherine A. Mulligan, BA; Scott McKnite, BS; Barry Detloff, BA; Paul Lindstrom, BS; and Karl H. Lindner, MD

Objectives: **This study was designed to assess whether intermittent impedance of inspiratory gas exchange improves the efficiency of standard cardiopulmonary resuscitation (CPR).**

Background: **Standard CPR relies on the natural elastic recoil of the chest to transiently decrease intrathoracic pressures and thereby promote venous blood return to the heart. To further enhance the negative intrathoracic pressures during the "relaxation" phase of CPR, we tested the hypothesis that intermittent impedance to inspiratory gases during standard CPR increases coronary perfusion pressures and vital organ perfusion.**

Methods: **CPR was performed with a pneumatically driven automated device in a porcine model of ventricular fibrillation. Eight pigs were randomized to initially receive standard CPR alone, while seven pigs initially received standard CPR plus intermittent impedance to inspiratory gas exchange with a threshold valve set to −40 cm H_2O. The compression:ventilation ratio was 5:1 and the compression rate was 80/min. At 7-min intervals the impedance threshold valve (ITV) was either added or removed from the ventilation circuit such that during the 28 min of CPR, each animal received two 7-min periods of CPR with the ITV and two 7-min periods without the valve.**

Results: **Vital organ blood flow was significantly higher during CPR performed with the ITV than during CPR performed without the valve. Total left ventricular blood flow (mean±SEM) (mL/min/g) was 0.32±0.04 vs 0.23±0.03 without the ITV ($p<0.05$). Cerebral blood flow (mL/min/g) was 20% higher with the ITV (+ITV, 0.23±0.02; −ITV, 0.19±0.02; $p<0.05$). Each time the ITV was removed, there was a statistically significant decrease in the vital organ blood flow and coronary perfusion pressure.**

Conclusions: **Intermittent impedance to inspiratory flow of respiratory gases during standard CPR significantly improves CPR efficiency during ventricular fibrillation. These studies underscore the importance of lowering intrathoracic pressures during the relaxation phase of CPR.**

(CHEST 1998; 113:1084-90)

Key words: active compression-decompression CPR; cardiac arrest; cardiopulmonary resuscitation; heart; impedance threshold valve; ventricular fibrillation

Abbreviations: ACD=active compression-decompression; CPP=coronary perfusion pressure; CPR=cardiopulmonary resuscitation; ITV=impedance threshold valve; NS=not significant

The potential value of increasing negative intrathoracic pressure during the decompression phase of cardiopulmonary resuscitation (CPR) with a new technique termed active compression-decompression (ACD) CPR has been described recently.[1-5] ACD CPR enhances the bellows-like action of the chest. Use of this method is associated with improved hemodynamic status in animal models and humans when compared with conventional manual CPR.[1-5] More recently, we demonstrated that the efficacy of ACD CPR could be further improved by insertion of an inspiratory impedance threshold valve (ITV) into the respiratory circuit.[6] In a porcine model of ventricular fibrillation, we observed that use of the ITV during ACD CPR, which physiologically mimics the clinical Müeller maneuver, lowers intrathoracic pressure during the decompression phase, thereby enhancing vital organ blood flow and lowering defibrillation energy requirements when compared with ACD CPR alone.[6] In the present study, we hypothesized that the use of an inspiratory

*From the Cardiac Arrhythmia Center (Dr. Lurie, Ms. Mulligan, and Messrs. McKnite, Detloff, and Lindstrom), Cardiovascular Division, University of Minnesota, Minneapolis, and the Department of Anesthesiology and Critical Care Medicine (Dr. Lindner), University of Ulm, Ulm, Germany.

Supported by the American Heart Association.

Manuscript received April 16, 1997; revision accepted September 10, 1997.

Reprint requests: Keith Lurie, MD, UMHC, Box 508, 420 Delaware Street SE, Minneapolis, MN 55409

impedance valve during standard closed-chest CPR, which also relies on the bellows-like action of the thorax, would enhance the negative intrathoracic pressure generated by the natural recoil of the chest during the decompression phase. As such, the purpose of the present investigation was to test this hypothesis by insertion of an inspiratory ITV into the respiratory circuit. We describe the measurements of central aortic pressures, coronary perfusion pressures, vital organ blood flow with radiolabeled microspheres, and arterial blood gases in a well-established porcine model of ventricular fibrillation.

Materials and Methods

Experiments described in this report were approved by the Committee on Animal Experimentation at the University of Minnesota. Healthy domestic female farm pigs (28 to 33 kg) were fasted overnight and anesthetized with pentobarbital, as previously described.[1,6] The anesthetic and surgical approach during the preparatory phase have also been described recently.[1,6] Left ventricular and ascending aortic arch BPs as well as right atrial pressures were monitored using high-fidelity micromanometer catheters (Millar Instruments; Houston). A single aorta-left ventricular micromanometer catheter with a lumen for injecting radiolabeled microspheres was used. A 5F bipolar pacing catheter (Daig Inc; Minnetonka, Minn) was used to induce ventricular fibrillation.[6] Core temperatures were maintained between 36.5 and 38.5°C. Fifteen minutes prior to induction of ventricular fibrillation, 5,000 U of sodium heparin was administered IV.

Closed-chest CPR was performed with a 6.5-cm circular compression pad positioned over the sternum. The automated device and the measurement of hemodynamic parameters have been described previously.[1,6] Compression and decompression excursion was measured continuously by the voltage output of a linear variable differential transformer.[6] Compression-decompression forces were similarly monitored continuously using a piezo electric force transducer.[6] These data, which included all hemodynamic measurements, assessment of the distal tracheal pressure from a fluid-filled pressure transducer connected to the distal end of the endotracheal tube, and measurements of compression/decompression chest excursion and compression/decompression forces, were digitized on-line (SUPERSCOPE II v.295; GW Instruments; Somerville, Pa) and analyzed electronically using a computerized recording system (Power Macintosh 7100/66 computer; Apple Computer; Cupertino, Calif).[6]

The protocol was designed to compare standard CPR alone with standard CPR plus an inspiratory ITV. Each pig served as its own control. The experimental protocol is seen in the schematic in Figure 1.

Once catheters were placed into the left ventricle, right atrium, and aorta, the right atrial diastolic pressures were maintained at 2.5 to 5 mm Hg with IV normal saline solution. Within 10 min of inducing ventricular fibrillation, the first radiolabeled microsphere was injected into the left ventricle to measure baseline blood flows. Once the reference arterial blood was collected, ventricular fibrillation was induced with a single 3- to 5-s application of alternating current directly to the right ventricle via the pacing catheter. The point at which ventricular fibrillation was induced was termed "time 0." At this point, the pigs were assigned randomly to initially receive either CPR alone or CPR plus the ITV. The endotracheal tube (ET tube high-low JET, Mallinckrodt Inc; St. Louis) was immediately disconnected from the mechanical ventilator and the tube cuff pressure was assessed to ensure that it was adequate to seal the trachea. After 3 min of ventricular fibrillation, during which time no chest compressions or ventilation was performed, CPR was initiated with the automated device. The compression rate was 80/min with a 50% duty cycle, a depth of 25% of the anterior-posterior diameter of the chest wall, and a velocity of 7.5 inches/s. Active upward movement of the compression pad was performed with the same velocity as during the compression phase such that it did not impede the natural recoil of the chest. Compression and decompression excursion was continuously monitored and adjusted with a control module to ensure that compression depth was adequate and that during the decompression phase the pad did not impede chest wall relaxation.[6]

Ventilatory support and automated standard CPR were performed simultaneously during CPR. Ventilation was provided by manual bag ventilation (Ambu bag; Glostrup, Denmark) and oxygen (8 L/min) as previously described.[3] Ventilatory support was continued throughout all experiments using manual bag ventilation with 10 L oxygen supplementation. Hand-held ventilation was utilized after preliminary experiments showed that it was easier to interpose manual ventilatory efforts at the end of the decompression phase with the bag ventilation than with mechanical ventilation. Moreover, the mechanical ventilators available to us (including the Harvard animal ventilator [Harvard Apparatus; Dover, Mass] and the Siemens ventilator [Siemens; Munich Germany]), which we have previously used,[1,3,6] had a significant amount of resistance to inspiration. That inspiratory resistance prevented us from testing our overall hypothesis. During CPR, respirations were delivered continuously at a rate of 16/min (one breath every five chest compressions) at a constant tidal volume of approximately 450 mL. As previously described, ventilations were delivered during the decompression phase of CPR.[1,6]

The ITV in this study consisted of two 20 cm H_2O threshold valves (Ambu Anesthesia PEEP Valve 20, No. 194011000; Ambu, Inc; Glostrup, Denmark) connected in series between the endotracheal tube and the Ambu bag such that during the decompression phase, but in the absence of manual ventilation, the valves opened only with greater than -40 cm H_2O of inspiratory pressure. In this fashion, more than -40 cm H_2O of intrathoracic pressure was required for inspiration of respiratory gases during four of every five compression cycles during performance of CPR with the ITV. With standard CPR and without active bag ventilation, use of these threshold valves in series resulted in effectively no inspiratory movement of respiratory gases during the decompression phase of CPR. As shown in the protocol time line, at 7-min intervals, the ITV was either added or removed

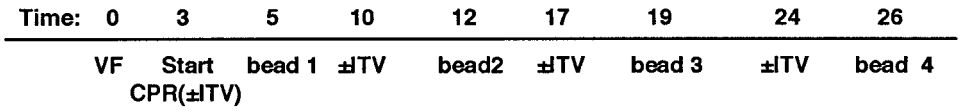

Figure 1. Experimental protocol.

from the ventilation circuit such that during the 28 min of CPR, each animal received two 7-min periods of CPR with the valve and two 7-min periods without the valve.

Once CPR alone or CPR plus the ITV was initiated, the same method was performed continuously for 7 min. Radiolabeled microspheres (beads 1 to 4) were injected 2 min after either insertion or removal of the ITV as previously described.[3,6] Arterial blood gasses were measured immediately prior to induction of ventricular fibrillation and then at the intervals shown in protocol schematic.

Myocardial and brain blood flows were determined with radiolabeled microspheres as previously described.[3,6]

Statistical analysis was performed using the unpaired and, when appropriate, paired Student's *t* test. The data that were not normally distributed were analyzed with the Mann-Whitney test for unpaired comparisons and the Wilcoxon signed rank test for paired comparisons. Statistical significance was considered to be at the $p<0.05$ level. All values are expressed as mean±SEM.

Results

Seven pigs were randomized to initially receive CPR with the ITV and eight pigs received CPR initially without the ITV. There were no significant differences in the compression forces between groups (ITV, 18.09±1.8 kg; no ITV, 18.63±1.75 kg). Similarly, there were no differences in compression depth between two groups (ITV, 6.2±0.1 cm; no ITV, 6.1±0.1 cm). Measurement of the mean intrathoracic pressures using the distal port of the endotracheal tubes demonstrated that pressures were lower in the presence of the ITV (−5.2±0.81) when compared with no ITV (−1.2±0.47) during the decompression phase ($p<0.001$).

Hemodynamic measurements were obtained at the time the radiolabeled microspheres were injected during each portion of the study. These data are shown in Table 1 and Figure 2. Prior to initiation of ventricular fibrillation, the aortic and right atrial pressures were similar between both groups. In pigs initially assigned to treatment with the ITV, the systolic aortic pressures were 114±6 vs 104±7 in the group assigned initially to no ITV (p, not significant [NS]). Similarly, the right atrial pressures were 3.0±0.5 in the group initially treated with the ITV vs 3.1±0.4 in the group assigned initially to no ITV (p, NS). Baseline myocardial and cerebral blood flows were similar as well. In pigs assigned to the ITV initially, the total left ventricular and cerebral blood flows during sinus rhythm in the baseline state were 1.42±0.11 mL/min/g and 0.33±0.05 mL/min/g, respectively, vs 2.15±0.38 mL/min/g and 0.44±0.06 mL/min/g, respectively, in pigs initially treated without the ITV (p, NS for cardiac or cerebral blood flow). When the blood flows were normalized to the baseline systolic aortic pressures (blood flow [mL/min/g]/aortic pressure [mm Hg]), there were no significant differences between the groups. The cardiac and cerebral values for the group that received ITV first were 75±6 and 256±36, respectively, vs 73±18 and 350±43, respectively, in the group that started without the ITV.

During performance of CPR, there were no significant differences in aortic systolic pressure during the compression phase of CPR when the ITV was

Table 1–*Hemodynamic Measurements

	2 min		9 min		16 min		23 min	
	−ITV	+ITV	−ITV	+ITV	−ITV	+ITV	−ITV	+ITV
Systolic								
LV	53.1±3.5	63.2±10.5	47.4±7.1	56.4±8.1	49.5±8.8	42.2±5.1	35.0±4.2	46.5±7.0
AO	50.4±2.9	60.3±8.1	43.5±5.2	51.6±6.8	45.1±6.2	41.8±3.5	35.5±30	43.4±5.9
RA	51.5±5.2	61.8±11.3	48.7±7.4	58.7±8.6	49.6±8.3	44.2±5.8	36.6±3.8	46.8±6.7
CPP	−1.1±4.6	−1.8±4.1	−4.6±3.8	−7.1±3.6	−4.4±3.1	−2.3±4.4	2.6±5.5	−3.4±2.7
Diastolic								
LV	13.0±1.4	15.1±2.8	10.8±2.8	9.8±1.4	9.0±1.0	9.1±2.7	8.5±2.9	9.0±1.1
AO	26.2±1.3	35.0±4.9	23.6±1.7	23.6±1.8	20.3±0.9	22.9±2.4	19.3±2.4	20.2±1.0
RA	10.9±1.3	13.7±2.6	10.2±1.2	10.0±1.7	9.0±1.5	9.0±1.1	7.6±0.8	8.1±1.7
CPP	15.3±1.5	20.3±3.8	13.4±1.4	13.6±1.7	11.3±1.7	13.0±2.7	11.4±2.6	12.1±1.9
	3 min		10 min		17 min		24 min	
	−ITV	+ITV	−ITV	+ITV	−ITV	+ITV	−ITV	+ITV
ABG								
pH	7.41±0.3	7.44±0.03	7.48±0.06	7.33±0.04†	7.33±0.06	7.43±0.04†	7.43±0.06	7.28±0.07†
P_{CO_2}	35.4±0.03	33.5±3.7	27.0±4.0	38.1±5.1†	36.0±6.8	29.1±3.5	28.7±4.5	40.3±0.07†
P_{O_2}	227±45	201±41	305±59	186±47	212±55	168±61	215±73	162±4.62

*LV=left ventricle; AO=aorta; RA=right atria; ABG=arterial blood gas; −ITV, standard CPR alone; +ITV, standard CPR plus the ITV; all data expressed as mm Hg±SEM.

†$p<0.05$ between groups at the time point.

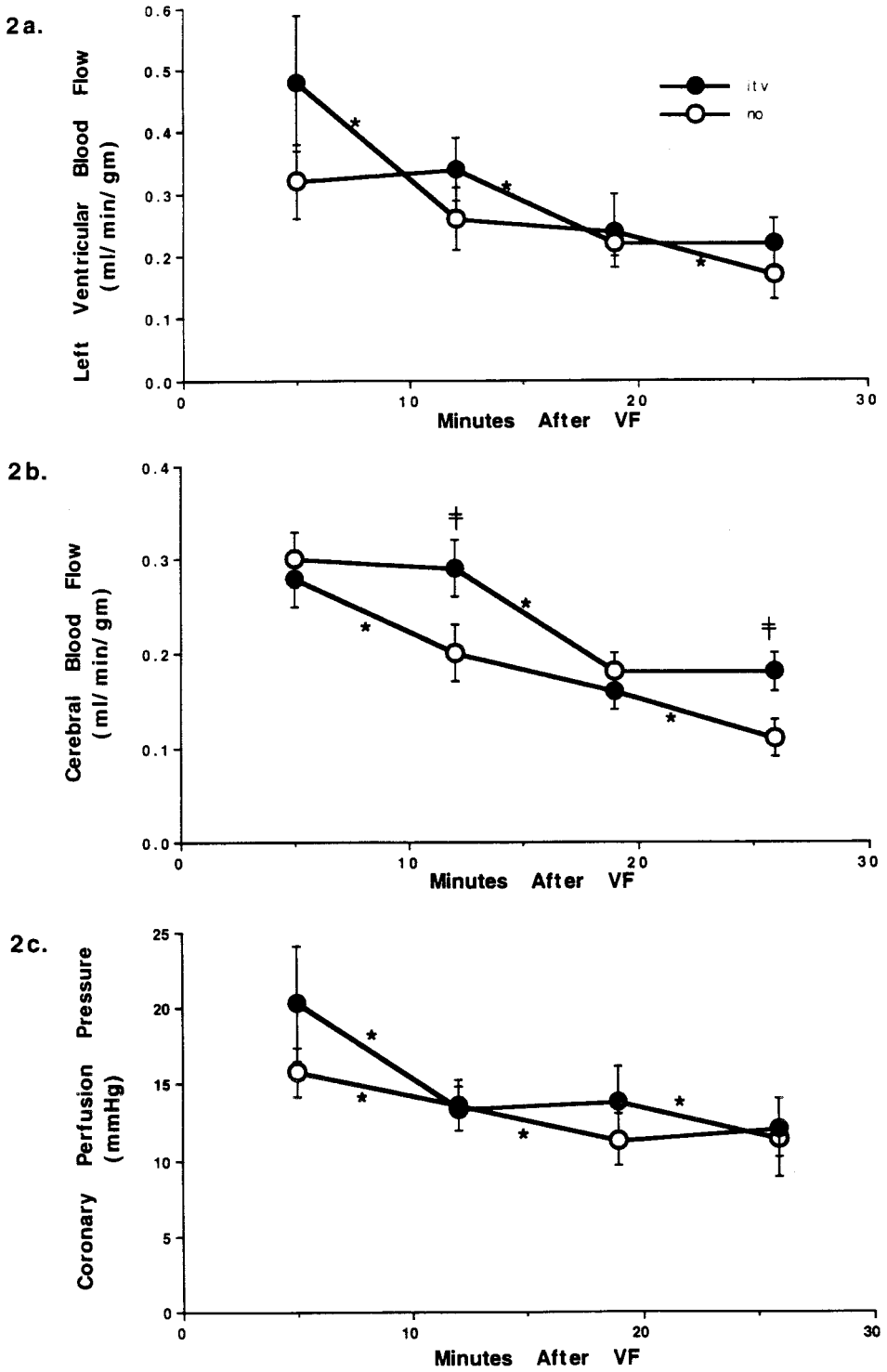

FIGURE 2. *Top (a)*: myocardial blood flow (mean±SEM) assessed 2, 9, 16, and 23 min after initiation of either standard CPR alone (open circles) or standard CPR plus the ITV (closed circles). After 7 min of CPR, the ITV was either added to or removed from the ventilatory circuit. Asterisk indicates $p<0.05$. *Center (b)*: brain blood flow (mean±SEM) assessed 2, 9, 16, and 23 min after initiation of either standard CPR alone (open circles) or standard CPR plus the ITV (closed circles). After 7 min of CPR, the ITV was either added to or removed from the ventilatory circuit. Asterisk indicates $p<0.05$ when analyzing the change in blood flow at different time points; double daggers indicate $p<0.05$ for the blood flow at a given time point. *Bottom (c)*: the mean (±SEM) CPP was calculated by the difference between the diastolic aortic and right atrial pressures 2, 9, 16, and 23 min after initiation of either standard CPR alone (open circles) or standard CPR plus the ITV (closed circles). After 7 min of CPR, the ITV was either added to or removed from the ventilatory circuit. Asterisk indicates $p<0.05$.

used (Table 1). Differences in the coronary perfusion pressures (CPPs) (diastolic aortic-right atrial pressures) were small between the two groups but trended higher when the ITV was used (Table 1 and Figs 3 and 2*c [bottom]*). The mean CPP during the entire 28 min of CPR tended to be higher during CPR with the ITV (14.8±1.3) than during CPR without the ITV (12.5±1.5; p=0.07).

In both groups (+ITV first and −ITV first), there was a significant decrease in CPP each time that the ITV was removed (Table 1 and Fig 2*c [bottom]*). In other words, there was a small yet statistically signifi-

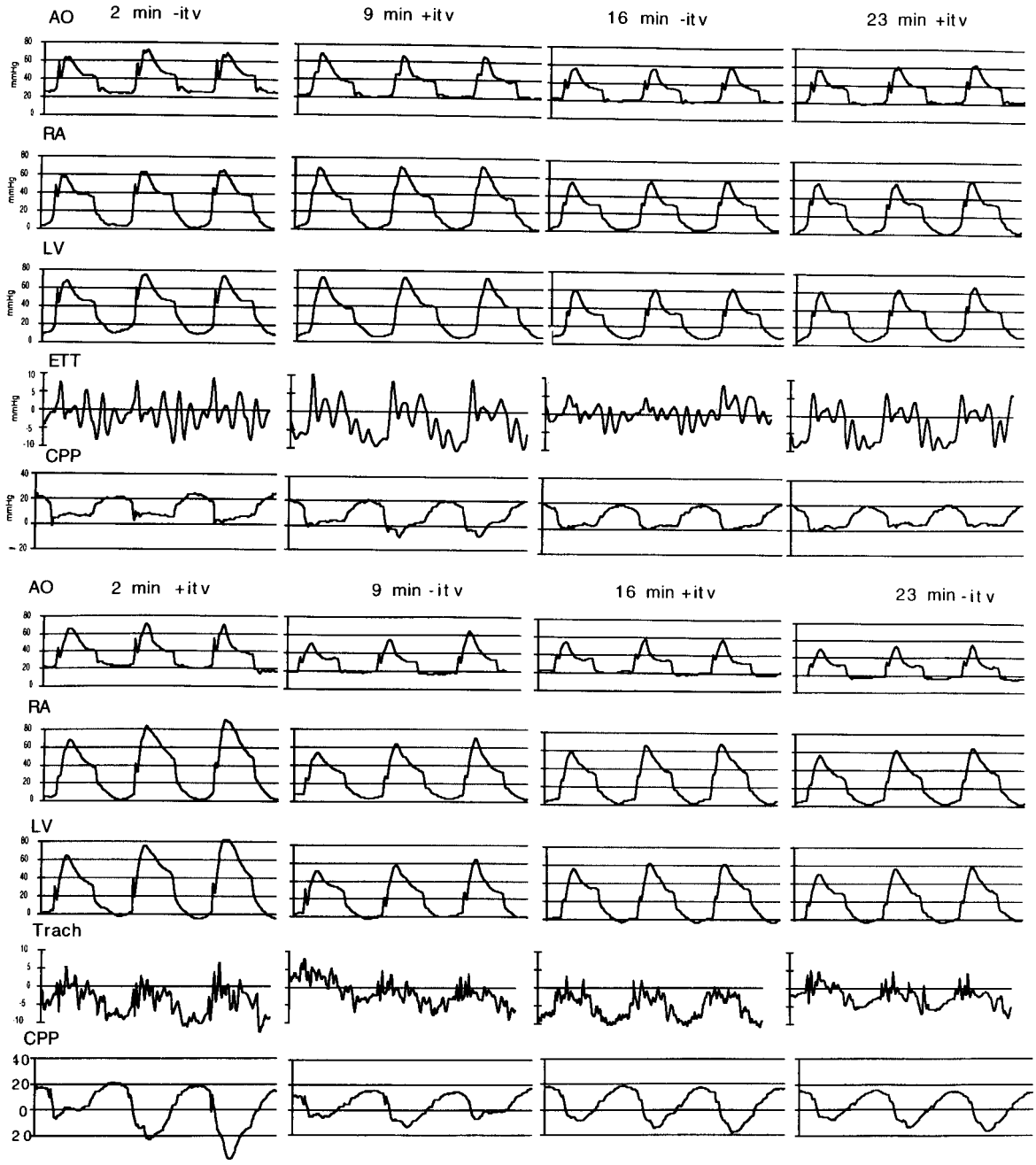

FIGURE 3. Aortic (AO), left ventricular (LV), right atrial (RA), CPPs (diastolic aortic minus right atrial pressures), and distal endotracheal tube (ETT) pressures (in mm Hg) from two representative studies comparing standard CPR alone (−ITV) with standard CPR plus the ITV in pigs in ventricular fibrillation. The ITV was set to open when negative intrathoracic pressure exceeded 40 cm H_2O. In the experiment shown in Figure 2 (*top*), the ITV was initially absent. In the experiment shown in Figure 2 (*center*), the ITV was initially present.

cant decrease in the CPP each time the ITV was removed from the respiratory circuit (Fig 2*c [bottom]*). In contrast, each time the ITV was added to the respiratory circuit, the mean CPP remained constant.

Use of the ITV during standard CPR also increased vital organ blood flow. The mean ventricular blood flow throughout the entire experiment was significantly higher during CPR+ITV than during CPR−ITV (+ITV, 0.32±0.04; −ITV, 0.23±0.03; $p<0.05$). Consistent with the measurement of the CPP, each time that the ITV was removed from the respiratory circuit, there was a statistically significant decrease in the left ventricular blood flow within that group (Fig 2*a [top]*).

In a similar manner, the mean cerebral blood flow throughout the entire experiment was significantly higher during CPR with the valve when compared with no valve (+ITV, 0.23±0.02; −ITV, 0.19±0.02; $p<0.05$). The cerebral blood flow was significantly higher during CPR with the ITV than without the ITV at two of the four time points (Fig 2*b [center]*). At the 12-min time point, cerebral blood flow was 50% higher with the ITV. As with the changes in CPP, in both groups (+ITV first and −ITV first), the cerebral blood flow significantly decreased within the group each time the ITV was removed (Fig 2*b [center]*).

The ratio between endocardial and epicardial blood flow was also examined. The mean endocardial/epicardial ratio throughout the experiment was significantly higher during CPR with the ITV (0.95±0.11) than without the ITV (0.81±0.09; $p<0.05$).

Arterial blood gas data are also shown in Table 1. Before ventricular fibrillation, baseline blood gases were similar between groups ($pH/Pco_2/Po_2$ were 7.41±0.01/43.1±1.9/170.4±21.5 in the ITV group and 7.40±0.02/41.0±2.6/179±20.4 in the no ITV group, respectively). There were no statistically significant differences in the Po_2 between groups at any time point. At 9, 16, and 23 min, the pH was significantly higher in the group that started initially with CPR+ITV. Correspondingly, at 9 and 23 min, the Pco_2 was significantly lower in the group that started CPR+ITV.

Discussion

Closed chest manual cardiac massage or standard CPR depends, in part, on the natural resilience of the chest wall to refill the heart with blood following each compression phase. This transient period of negative intrathoracic pressure is a critical aspect of any method of CPR. When the inflow of respiratory gases is impeded by an inspiratory threshold valve, equilibration of the negative intrathoracic pressure generated by the elastic recoil of the chest occurs to a greater extent by enhanced venous return and not by movement of respiratory gases. Results from the current study demonstrate that myocardial perfusion is increased by 40% during standard CPR in the presence of the ITV compared with standard CPR alone. The results further suggest that endocardial blood flow is increased with the use of the ITV. Overall, these results imply that insertion of an ITV into the respiratory circuit during standard CPR enhances the return of venous blood to the thoracic area. These findings are consistent with an earlier study in which the ITV was found to enhance the efficacy of ACD CPR.[6] Together, these investigations suggest that intermittent impedance to inspiration during a performance of any method of CPR, which relies at least in part on either passive or active elastic recoil of the chest wall to enhance venous return, should significantly increase overall CPR efficacy.

In this study, the beneficial effects of the ITV, as demonstrated by the prevention in a significant decrease in the CPP or vital organ perfusion when the ITV was added to the respiratory circuit, were most pronounced each time the ITV was removed from the respiratory circuit (Fig 2). Given the similar measurements of vital organ blood flow and CPP obtained 2 min after initiation of CPR between both groups, these results suggests that other factors, in particular the initial profound neurohormonal response to cardiac arrest, may mask any potential initial beneficial effects of the mechanical augmentation in myocardial perfusion with the ITV. We have previously observed that there is an outpouring of stress hormones that increase systemic pressures in the first several minutes after an arrest.[7] The results of the present study also suggest that the potential benefit of the ITV may depend on the changes in myocardial compliance and alterations in intravascular volume that occur over time after cardiac arrest.

The relationship between the calculated coronary perfusion pressure and myocardial blood flow in this study was not 1:1. Use of the ITV increased the calculated coronary perfusion pressure by about 2 to 5 mm Hg, an overall percentile increase of approximately 20%. In contrast, myocardial perfusion was increased by 40% during the same time interval. These findings suggest that changes in CPP underestimate the potential benefit of the ITV. Moreover, they suggest that there is a minimum negative intrathoracic pressure threshold during the decompression phase that must be overcome, at which point myocardial perfusion increases in a nonlinear rate. In this fashion, the increase in negative intrathoracic pressure during

the decompression phase appears to "afterload" the left and right heart, facilitating venous return and coronary perfusion without a significant change in overall systolic pressures. The mechanisms responsible for this graded increase in myocardial perfusion remain unknown but may include the relative gradients between the aorta and left ventricular end-diastolic pressure, hydrostatic gradients between the arterioles and the interstitium, the relative rates of right heart filling at a given negative intrathoracic pressure, and the relative responsiveness of the arterial and venous tree to subtle shifts in maximal negative intrathoracic pressure.

Despite our current inability to fully understand the physiologic factors involved in enhancement of myocardial perfusion with the ITV, the results highlight the potential value of maximizing efforts to decrease negative intrathoracic pressure during the decompression or "relaxation" phase of CPR to enhance overall venous return and ultimately cardiac perfusion and overall CPR efficacy. Increasing negative intrathoracic pressures during the decompression, in addition to efforts aimed at maximizing positive intrathoracic pressures during the compression phase, appears to be important when optimizing the potential mechanical benefits of closed chest cardiac massage. Although pharmacologic therapy can be used to increase systemic arterial pressures, augmentation of right heart filling is an essential part of CPR. Enhancement of right heart filling, though difficult to assess by measurement of the calculated CPPs *per se*, can be indirectly measured using radiolabeled microspheres to quantitate total myocardial blood flow. In a clinical analogy to the treatment of a right ventricular infarction, enhanced blood flow to the right side of the heart is essential for maintenance of adequate cardiac perfusion and cardiac output during both a right ventricular infarction as well as during cardiac arrest. Based on the present study, maximizing negative intrathoracic pressure during the decompression phase of CPR appears to be an effective way to help increase right heart filling and overall venous return.

The potential value of enhancing of negative intrathoracic pressure during passive relaxation of the chest wall by the use of an ITV is highly dependent on chest wall compliance, fluid status, diaphragmatic tone, as well as size of the heart and the compliance of the ventricular wall. Use of an impedance valve during CPR serves to "prime the pump" and is one of several new techniques available to enhance venous return to the heart during cardiac arrest and CPR. Although venous return during "optimal" mechanical CPR may be provided by the combination of the ITV and ACD CPR,[6] the present study suggests that even in the absence of new CPR techniques, the ITV holds potential promise to improve the efficacy of standard CPR.

ACKNOWLEDGMENT: The authors would like to thank Gail Rosenbaum for her assistance in preparing this manuscript.

References

1 Lindner KH, Pfenninger E, Lurie KG, et al. Effects of active compression-decompression resuscitation on myocardial and cerebral blood flow in pigs. Circulation 1993; 88:1254-63
2 Cohen TJ, Tucker KL, Lurie KG, et al. Active compression-decompression: a new method of cardiopulmonary resuscitation. JAMA 1992; 267:2916-23
3 Chang MW, Coffeen P, Lurie KG, et al. Active compression-decompression CPR improves vital organ perfusion in a dog model of ventricular fibrillation. Chest 1994; 106:1250-59
4 Lurie KG. Active compression-decompression, cardiopulmonary resuscitation: a progress report. Resuscitation 1994; 28:115-22
5 Guly UM, Robertson CE. Active decompression improves the haemodynamic state during cardiopulmonary resuscitation. Br Heart J 1995; 73:372-76
6 Lurie KG, Coffeen P, Shultz J, et al. Improving active compression-decompression cardiopulmonary resuscitation with an inspiratory impedance valve. Circulation 1995; 91: 1629-32
7 Lindner KH, Haak T, Keller A, et al. Release of endogenous vasopressors during and after cardiopulmonary resuscitation. Br Heart J 1996; 75:145-50