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Effect of an inspiratory impedance threshold device on hemodynamics during conventional manual cardiopulmonary resuscitation☆,☆☆

Ronald G. Pirrallo[a,*], Tom P. Aufderheide[a], Terry A. Provo[b], Keith G. Lurie[b,c]

[a] *Medical College of Wisconsin, Department of Emergency Medicine, 9200 W. Wisconsin Ave., FEH Room 1870, Milwaukee, WI 53226, USA*
[b] *Advanced Circulatory Systems Inc., 7615 Golden Triangle Dr., Suite A, Eden Prairie, MN 55344, USA*
[c] *Department of Emergency Medicine, Hennepin County Medical Center, Minneapolis, MN, USA*

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Abstract

Background: In animals in cardiac arrest, an inspiratory impedance threshold device (ITD) has been shown to improve hemodynamics and neurologically intact survival. The objective of this study was to determine whether an ITD would improve blood pressure (BP) in patients receiving CPR for out-of-hospital cardiac arrest.
Methods: This prospective, randomized, double-blind, intention-to-treat study was conducted in the Milwaukee, WI, emergency medical services (EMS) system. EMS personnel used an active (functional) or sham (non-functional) ITD on a tracheal tube on adults in cardiac arrest of presumed cardiac etiology. Care between groups was similar except for ITD type. Low dose epinephrine (1 mg) was used per American Heart Association Guidelines. Femoral arterial BP (mmHg) was measured invasively during CPR.
Results: Mean ± S.D. time from ITD placement to first invasive BP recording was approximately 14 min. Twelve patients were treated with a sham ITD versus 10 patients with an active ITD. Systolic BPs (mean ± S.D.) [number of patients treated at given time point] at $T = 0$ (time of first arterial BP measurement), and $T = 2$, 5 and 7 min were 85 ± 29 [10], 85 ± 23 [10], 85 ± 16 [9] and 69 ± 22 [8] in the group receiving an active ITD compared with 43 ± 15 [12], 47 ± 16 [12], 47 ± 20 [9], and 52 ± 23 [9] in subjects treated with a sham ITD, respectively ($p < 0.01$ for all times). Diastolic BPs at $T = 0$, 2, 5 and 7 min were 20 ± 12, 21 ± 13, 23 ± 15 and 25 ± 14 in the group receiving an active ITD compared with 15 ± 9, 17 ± 8, 17 ± 9 and 19 ± 8 in subjects treated with a sham ITD, respectively (p = NS for all times). No significant adverse device events were reported.
Conclusions: Use of the active ITD was found to increase systolic pressures safely and significantly in patients in cardiac arrest compared with sham controls.

Keywords: Blood pressure; Cardiac arrest; Cardiopulmonary resuscitation; Circulation; Impedance threshold device; Emergency medical services

1. Introduction

The objective of cardiopulmonary resuscitation (CPR) is to provide sufficient circulatory support to a patient in cardiac arrest to restore spontaneous circulation. The cornerstone of this approach is maintenance of an adequate blood pressure and vital organ perfusion pressure when the heart is incapable of providing that essential cardiac output on its own. The concept of providing inspiratory impedance during the decompression phase of CPR as a means to improve its efficacy was first introduced in 1995. [1] By impeding the influx of respiratory gases into the chest selectively during the decompression (or chest wall recoil) phase of CPR, negative intrathoracic pressure is enhanced, resulting in improved venous return (cardiac preload) and thus, improved blood pressure and cardiac output.

Animal studies have shown that use of an inspiratory impedance threshold device (ITD) within the respiratory circuit during both conventional CPR and active

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* Corresponding author. Tel.: +1 414 805 6456; fax: +1 414 805 6464.
E-mail address: pirrallo@mcw.edu (R.G. Pirrallo).

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compression–decompression (ACD) CPR increases blood flow to the heart and brain [1–4] and increases 24-h survival and improves neurological recovery [5]. Studies have also shown the benefit of an ITD on hemodynamics and short- and longer-term outcomes in humans receiving ACD CPR [6–8]. To date, there are no published reports on the hemodynamic effects of using the ITD during conventional CPR in humans. Thus, the purpose of this prospective, randomized, controlled, double-blind, intention-to-treat study was to measure changes in blood pressure (BP) in patients with an out-of-hospital cardiac arrest who received conventional manual CPR either with or without inspiratory impedance.

2. Material and methods

This study was performed in an out-of-hospital setting in the city of Milwaukee (WI) with a population of about 600,000 people and an area of about 100 square miles. Emergency medical services (EMS) are provided by the city's full-time fire department in a two-tiered manner, with firefighters cross-trained as emergency medical technicians providing basic life support (BLS) care and paramedics providing advanced life support (ALS) care consistent with American Heart Association (AHA) and ILCOR guidelines [9].

The United States Food and Drug Administration (FDA) approved an investigational device exemption for this study. The Medical College of Wisconsin's Institutional Review Board (IRB) and seven other IRBs representing 13 area receiving hospitals approved the study as well. The FDA approved an *Exception from Informed Consent Requirements for Emergency Research* as permitted by 21 CFR Subpart B, Section 50.24, which required investigators to meet the requirements for: (1) community consultation, (2) public disclosure, (3) establishment of an independent data monitoring committee, (4) subsequent subject notification, and (5) informed consent for continued participation in the trial for survivors. An independent Clinical Events Committee and Data and Safety Monitoring Board were established to adjudicate and monitor adverse events, provide guidance on subject inclusion and exclusion, and monitor endpoints.

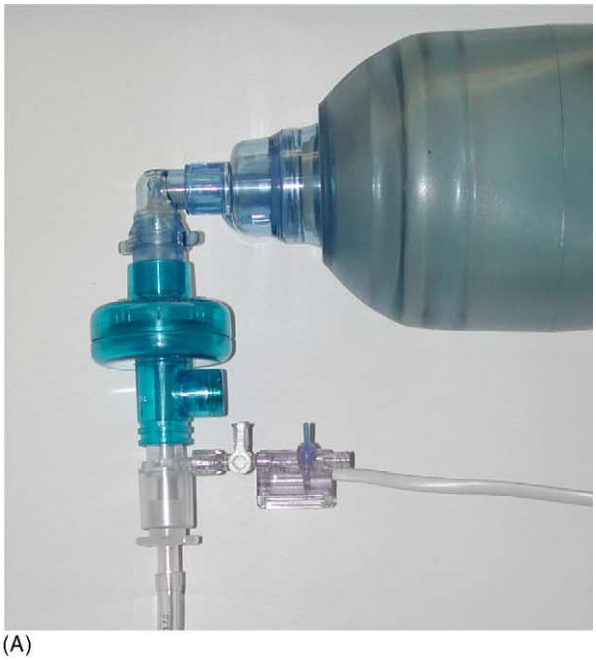
The primary endpoint was invasive femoral arterial blood pressure. The small sample size dictated by the investigational device exemption necessitated calculation based upon an anticipated 60% increase in systolic blood pressure (mmHg) in the active ITD group and an anticipated systolic blood pressure of approximately $50 \pm 10\%$ in the control group [10] to 80 ± 8 in the experimental treatment group. A total of 10 subjects per group were needed to demonstrate an absolute change of 60% with an α of 0.2, a power of 80%, and statistical significance with a p-value of 0.05. Secondary endpoints included the measurement of diastolic blood pressure, end tidal carbon dioxide and oxygen saturation. Data were collected prospectively according to the recommendations of the Utstein template for CPR research [11].

A hemodynamic research team, consisting of an emergency medicine trained physician and paramedic, was assembled for this study. This team worked along side of EMS providers who normally respond to the call for help. The research team was dispatched via a separate emergency vehicle during normal weekday business hours. Standard cardiac arrest treatment was provided by EMS personnel, including low dose epinephrine (adrenaline) (1 mg), performance of conventional manual CPR for a minimum of 30 min per patient, basic and advanced life support care, capnography and defibrillation as indicated, and airway management that generally began with bag-valve mask ventilation, followed by the insertion of a tracheal (ET) tube. EMS personnel were responsible for providing routine resuscitation care while the research team was primarily responsible for the collection of additional hemodynamic data. However, after the early recognition that EMS personnel were providing excessive ventilation rates during CPR [12], the research team paramedic was given the additional responsibility to serve as a study monitor. After a 1-min period to evaluate the quality of CPR, this paramedic monitor provided feedback to EMS personnel regarding CPR compression rate, depth, adequacy of chest wall recoil, ventilation rate and ventilation duration. In this manner, we attempted to control for the quality of CPR throughout the study.

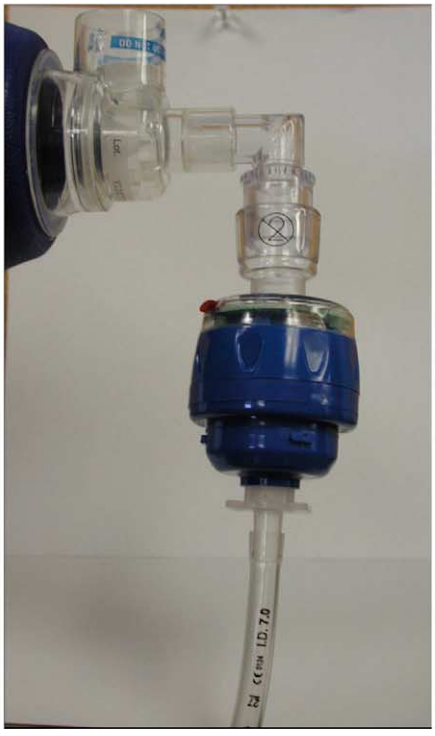
The research team responded to the scene of all adult patients who presented with an out-of-hospital cardiac arrest of presumed cardiac etiology in the city of Milwaukee when they were on call. Patients in whom a tracheal tube was successfully placed in the trachea (as confirmed by end tidal carbon dioxide monitoring) were randomized to receive conventional manual CPR with either an active (functional) or sham (non-functional) ITD (Advanced Circulatory Systems Inc., Eden Prairie, Minnesota, USA) upon arrival of the advanced life support team at the scene. The ITD was placed within the respiratory circuit, between the tracheal tube and the bag-valve resuscitator. EMS personnel were instructed to ventilate and perform CPR according to American Heart Association Guidelines. Rescuers were instructed to remove the ITD during periods of return of spontaneous circulation (ROSC) and/or upon arrival at the receiving emergency department.

Devices were used in a computer-generated, randomized order. Active ITDs provided inspiratory impedance by not permitting inspiratory airflow unless a pressure of at least -16 cm H_2O was generated at the patient port. The ITD added approximately 45 mL of dead space to the circuit. Neither device provided resistance to rescuer ventilation or exhalation by the subject. Sham ITDs were manufactured to appear externally identical, but internally were modified such that there could be no inspiratory impedance. As such, they essentially functioned as a hollow conduit to ventilatory gases. In this way, rescuers and investigators were blinded to the device function (active or sham). They remained blinded through subject follow-up and the data analysis phase of the study.

When the study began, neither the active nor the sham ITD (Fig. 1A) contained timing assist lights. Based upon the



(A)



(B)

Fig. 1. (A) Impedance threshold device (ResQValve) within the ventilation circuit (between the tracheal tube and ventilation bag). The pressure transducer for obtaining intratracheal pressures is shown in circuit. (B) Newer model impedance threshold device (ResQPOD®) within the ventilation circuit (between the tracheal tube and ventilation bag). This model includes ventilation timing assist lights.

observation that trained rescuers were providing excessive ventilation rates during CPR [12], after approximately 50% enrollment in this study, the study was temporarily halted. Investigators changed to a newer model of the ITD (Fig. 1B) that included ventilation timing assist lights, retrained EMS personnel on the importance of ventilation rate control and the importance of allowing the chest to recoil fully after each chest compression, and then resumed study enrollment. The new ITD with ventilation timing assist lights provided (or in the case of shams, did not provide) inspiratory impedance in the same functional manner as the original devices. The timing assist lights for both active and sham devices, when turned on, flashed at a rate of 12 min^{-1}, providing a guide to rescuers for proper ventilation rate.

Inclusion criteria included: (1) adults (known or presumed to be ≥21 years) who presented with cardiac arrest of presumed cardiac etiology and were receiving CPR by EMS personnel, (2) intubated subjects who could be effectively ventilated with a tracheal tube, and (3) ability to acquire at least 2 min of invasive femoral arterial blood pressure measurements during CPR. Exclusion criteria included: (1) subjects known or presumed to be <21 years, (2) subjects with suspected non-cardiac arrest etiology, (3) subjects unable to be tracheally intubated with a tracheal tube, (4) subjects with pre-existing *do not resuscitate* orders, and (5) subjects who were resuscitated or had resuscitation terminated prior to successful placement of all monitoring equipment.

End tidal carbon dioxide ($ETCO_2$) data were collected via an in-line airway sensor attached to an M Series CCT monitor (ZOLL Medical Corp.). Oxygen saturation was obtained via a sensor connected to the M Series CCT monitor and to the subject's finger or earlobe.

Upon arrival and verification of patient inclusion criteria, the hemodynamic research physician attempted to cannulate the femoral artery using a wire over the needle sterile technique. For each patient, a standard Arrow™ (Arrow International, Reading, PA, product number AK-0451) arterial line kit was matched with an Edwards™ (Edwards Lifesciences, LLC, Irvine, CA, model number PX600F) pressure transducer and zeroed to ambient pressure per manufacture recommendation prior to data acquisition. Once arterial access was achieved, the catheter was sutured in place and a sterile dressing applied.

Arterial blood pressure data were recorded on a continuous (minute by minute) basis. Mean blood pressure values were obtained once the arterial line was in place ($T = 0$) and then 2, 5 and 7 min later, and were analyzed and reported along with concurrent $ETCO_2$ and pulse oximetry measurements. Arterial waveform data were available to help guide clinical care decisions. If ROSC was achieved, CPR was discontinued and the ITD was removed. Subjects were then transported to the nearest hospital emergency department with the research physician in attendance. If ROSC did not occur, resuscitation was terminated in the field consistent with Milwaukee EMS system policy. EMS personnel and the research team monitored the subject for adverse events.

All values are expressed as mean ± standard deviation (S.D.). Statistical assessment of the endpoints was performed with the repeated measures analysis of variance. Statistical significance was considered to be $p < 0.05$. 95% confidence intervals (CIs) were calculated at $T = 0$, 2, 5 and 7 min follow-

ing successful placement of an invasive arterial blood pressure monitoring system.

3. Results

During the course of this study, a total of forty patients in cardiac arrest were treated with either a sham or an active ITD and had hemodynamic monitoring attempted. Eighteen patients did not meet study inclusion criteria for the following reasons: inability to obtain invasive blood pressure recordings during CPR for at least 2 min prior to ROSC or discontinuation of resuscitation efforts (active: 10; sham: 6), non-cardiac etiology of arrest (active: 1; sham: 0) and monitoring equipment malfunction (active: 0; sham: 1). Of the 22 successful cases, the research physician was able to cannulate the femoral artery successfully on the first attempt in three cases; the second attempt in five cases; and in ≥3 attempts in 14 cases. On average, 3.4 needle sticks were required in each treatment group in order to place the femoral arterial catheter successfully.

The clinical characteristics of the subjects enrolled in the study, as well as the response intervals by EMS for these patients, were similar between the included active and sham groups (Table 1). The mean ± S.D. interval (min) between 911 call and first invasive BP measured was 34.0 ± 11.0 in the active and 34.9 ± 10.5 in the sham group; $p = 0.84$. The average duration of ITD use prior to the first measurement of arterial pressure ($T = 0$) was 15.0 ± 12.6 min for the active and 13.6 ± 9.6 min for the sham ITD.

Hemodynamic results from blood pressure recordings of the 10 patients treated with an active ITD and 12 with a sham ITD are shown in Table 2. As resuscitation efforts progressed, there were fewer patients in whom data were available, as some had a return of spontaneous circulation and in the others the clinical team determined that further CPR was not warranted or justified. The initial systolic blood pressures were significantly higher in the active ITD group, as shown in Fig. 2A. Diastolic blood pressures were generally higher with the active ITD, but these differences did not achieve statistical significance (Fig. 2B). The numbers of patients in whom blood pressures were recorded during the study are shown at each time point in Fig. 2. Ventilation rates averaged between 11 and 14 breaths/min throughout the hemodynamic data acquisition time frame and these rates were statistically similar between the sham and active ITD treatment groups.

While the study was in progress the ITD was modified. Data were gathered from patients treated with an ITD with and without ventilation timing lights and results were similar in terms of the primary outcome measurements. Comparison of the two models of the ITD within the same treatment resulted in similar hemodynamic effects based upon differences in mean values. A two-factor (sham/active and device model, with interaction term) analysis of variance confirmed similar effects with the old and new devices with respect to changes in systolic blood pressure. However, there was less variability

Table 1
Subject characteristics (mean ± S.D. (or %))

	Sham ITD ($n = 12$)	Active ITD ($n = 10$)	p-Value
Age (years)	58.3 ± 18.9	64.6 ± 21.3	0.48
Males (%)	9 (75%)	4 (40%)	0.192
Height estimate (in.)	68.4 ± 3.9	66.8 ± 3.9	0.37
Weight estimate (lbs)	179.4 ± 36.6	199.5 ± 54.5	0.37
Initial cardiac rhythm (%)			0.326
V-fib or pulseless V-tach	1 (8%)	3 (30%)	0.293
Asystole	5 (42%)	5 (50%)	1.00
PEA	5 (42%)	2 (20%)	0.381
Unknown	1 (8%)	0 (0%)	1.0
PEA at any time during arrest (%)	4.2	30	0.675
Witnessed cardiac arrest (%)	6 (50%)	4 (40%)	0.691
Reported downtime if witnessed (min)	1.8 ± 2.6	9 ± 7.3	0.145
Bystander CPR (%)	3/9 (33%)	2/10 (20%)	0.628
ITD duration (min)	27.6 ± 11.4	28.0 ± 14.6	0.95
Total CPR duration (min)	43.8 ± 9.8	46.2 ± 9.8	0.56
Total epinephrine (adrenaline) dose (mg)	6.8 ± 2.2	6.3 ± 2.2	0.57
Vomiting during CPR (%)	2 (17%)	1 (10%)	1.0
ALS response time (min)	8.1 ± 5.2	9.4 ± 3.3	0.48
911 to research team arrival (min)	17.3 ± 9.7	14.8 ± 4.3	0.44
911 to time zero (min)	34.9 ± 10.5	34.0 ± 11.0	0.84
911 to ITD placement (min) (if available)	20.4 ± 5.6	18.1 ± 5.2	0.40
ITD use prior to time zero (min) (if defined)	13.6 ± 9.6	15.0 ± 12.6	0.81
ITD model received			0.391
ResQValve	4 (33.3%)	6 (60%)	
ResQPOD	8 (66.7%)	4 (40%)	

911: time of 911 call; ALS: advanced life support; CPR: cardiopulmonary resuscitation; ITD: impedance threshold device; PEA: pulseless electrical activity; S.D.: standard deviation; time zero: time invasive arterial pressure monitoring first confirmed; V-fib: ventricular fibrillation; V-tach: ventricular tachycardia.

Table 2
Endpoint data

	All subjects, all rhythms		
	Active ITD	Sham ITD	*p*-Value
Hemodynamics (mean ± S.D.)			
SAP (mmHg) at time zero	85.1 ± 28.9	42.9 ± 15.1	0.001
SAP (mmHg) at 2 min	84.9 ± 23.1	47.2 ± 16.4	0.0005
SAP (mmHg) at 5 min	84.5 ± 15.9	46.7 ± 20.3	0.003
SAP (mmHg) at 7 min	69.2 ± 22.2	52.1 ± 22.7	0.005
DAP (mmHg) at time zero	20.2 ± 11.7	15.2 ± 8.7	0.262
DAP (mmHg) at 2 min	21.0 ± 12.7	16.6 ± 8.2	0.359
DAP (mmHg) at 5 min	23.0 ± 14.6	16.8 ± 8.7	0.299
DAP (mmHg) at 7 min	25.0 ± 13.9	19.2 ± 7.7	0.315
SaO_2 (%) at time zero	59.7 ± 26.5	59.3 ± 22.9	0.979
SaO_2 (%) at 2 min	62.8 ± 16.8	56.6 ± 23.9	0.591
SaO_2 (%) at 5 min	52.6 ± 15.4	48.6 ± 18.4	0.654
$ETCO_2$ (mmHg) at time zero	23.7 ± 10.3	20.8 ± 11.8	0.621
$ETCO_2$ (mmHg) at 2 min	24.5 ± 10.6	20.9 ± 10.5	0.470
$ETCO_2$ (mmHg) at 5 min	26.6 ± 12.7	23.8 ± 10.7	0.638

DAP: diastolic arterial pressure; $ETCO_2$: end tidal carbon dioxide; ITD: impedance threshold device; SaO_2: oxygen saturation; SAP: systolic arterial pressure; S.D.: standard deviation.

in blood pressures in the sham treatment group when the timing lights were used. It is not known whether the decreased variability in the sham ITD group with the timing lights was due to a small sample size with the potential for a single outlier to increase variability, the device design with the presence of timing lights, or the presence of the paramedic monitor in all cases where the ITD with a ventilation timing light was used. End tidal carbon dioxide data were recorded in 20 of the 22 subjects enrolled in the study. Data could not be obtained in two subjects with an active ITD due to equipment malfunction. End tidal carbon dioxide values were compared between groups and the data analyzed as shown in Table 2. There was a non-statistically significant increase in $ETCO_2$ in patients receiving an active ITD.

Oxygen saturation data were recorded in 20 of the 22 subjects enrolled in the study. It could not be obtained consistently in two subjects (one active ITD, one sham ITD) as the minimum level of circulation needed to record oxygen saturation was not reached in these patients. These data are similar between treatment groups and are shown in Table 2.

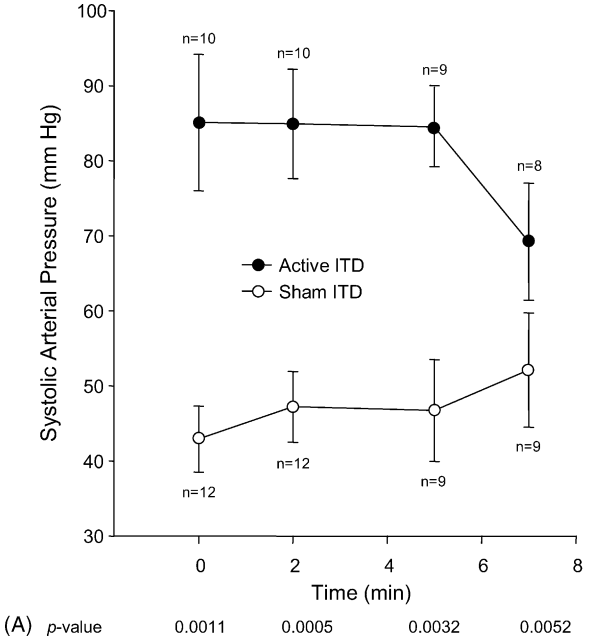
Review of the data revealed an additional important observation. There was a high incidence of "pseudo"-pulseless electrical activity (PEA) in the patient population studied [13]. That is, there was evidence of low amplitude increases in arterial blood pressure associated with each cardiac depolarization in half of the 22 subjects studied (four in the active ITD group, seven in the sham group) who had a rhythm of PEA at some time during the resuscitation effort. A representative tracing from a subject undergoing CPR with this pseudo PEA is shown in Fig. 3. In the absence of chest compressions, there was a rise in arterial blood pressure with each cardiac contraction, but the amplitude of the arterial pulse was too low to be detected by palpation of the femoral or carotid artery.

There were too few subjects in each group to draw any meaningful conclusions related to short-term survival endpoints. Only three patients treated with the sham ITD and two patients treated with the active ITD had a return of spontaneous circulation.

There were no clinically significant adverse events or complications in either group. Of the subjects who received an ITD and had a chest X-ray performed, pulmonary edema was reported in 3/5 sham cases and 1/2 active cases. In the 22 included cases, gastric regurgitation during ITD use was reported in 2/12 (17%) of the sham cases and 1/10 (10%) of the active group. There were no reported adverse events associated with hemodynamic monitoring in either group; there were no needle sticks or exposures to blood or body fluids of research team members. There was, however, a problem with the timing lights on some ITDs. Some lights did not turn on at all and in other cases the lights stopped flashing before the CPR efforts were completed. These issues were brought to the attention of the manufacturer who has since remedied this problem.

4. Discussion

These results demonstrate, for the first time, the hemodynamic benefits of using an ITD in patients undergoing standard CPR. Similar to recently described animal studies [2–5], use of an active ITD in patients undergoing external chest compressions resulted in an almost 100% increase in systolic arterial pressure when compared with sham controls at the initial time points. Diastolic blood pressures and $ETCO_2$ levels were increased in the active ITD group but the increase did not achieve statistical significance. The present study adds further support to our understanding of the fundamental physiology underlying hemodynamics during CPR and the resulting benefit of the impedance threshold device. By harnessing the kinetic energy associated with passive chest wall recoil, the ITD augments negative intrathoracic pressure during the decompression phase of CPR, thereby enhancing blood flow



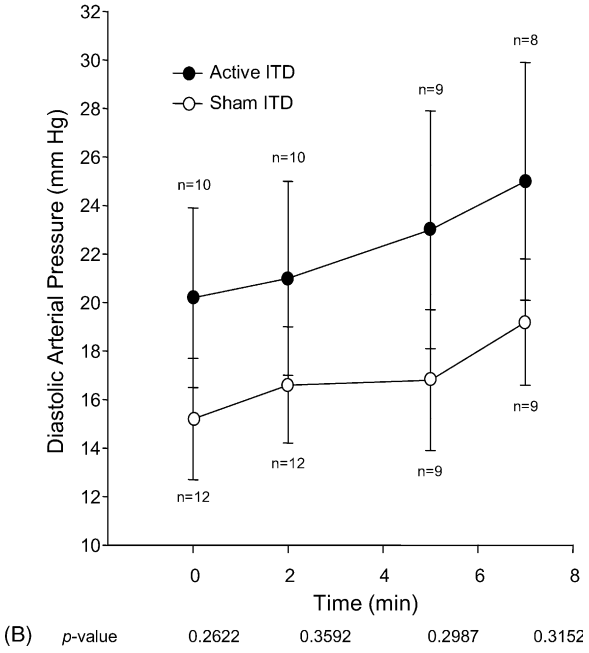


Fig. 2. $T = 0$ is the time when the first invasive blood pressure were recorded. On average, patients were treated with conventional CPR and the ITD for 14 min prior to $T = 0$ in both groups. The n values equal the number of patients with data recordings at any given time point. A minimum of 2 min of BP recordings were needed for enrollment. The n number decreased with time as some patients had a return of spontaneous circulation and resuscitative efforts were terminated in others.

back to the heart. The increase in preload results in increased cardiac output and higher blood pressures with each chest compression. As such, use of the ITD functions physiologically as a Muller maneuver [14] during the performance of CPR in patients in cardiac arrest.

The changes in blood pressure in the current study and in those during the use of active compression–decompression CPR correlate well with increased short-term survival rates observed in larger clinical trials [6–8]. For example, in a concurrent, randomized, blinded clinical trial focused on ICU admission rates in a similar patient population in Milwaukee, Wisconsin, survival rates were higher in patients treated with the ITD, especially in those who presented with PEA (over 100% increase in short-term survival) [15]. Similarly, the increase in blood pressure and coronary perfusion pressure with use of the combination of the ITD and active compression–decompression CPR in humans correlated well with the increased 24-h survival rates observed in two large randomized clinical trials [6–8]. As such, these data provide strong support for the use of blood pressure measurements as a good surrogate for at least short-term survival rates. Taken together, these trials support the widespread use of the ITD as an effective CPR adjunct that can increase circulation significantly and thus improve clinical outcomes for patients in cardiac arrest.

There is one new and important additional observation in the current study. There was a high incidence of low amplitude blood pressures associated with regular electrical activity in the absence of CPR. Similar to the representative example in Fig. 3, 11/22 of the patients studied were in pseudo PEA. They had hemodynamic and electrocardiographic evidence of a regular heart rhythm and a blood pressure that increased with each cardiac depolarization; however, that increase in blood pressure was insufficient to provide spontaneous and effective circulation without further CPR. It is unknown whether these low amplitude pressures represent weak left ventricular contractions or continued arterial contractions in the absence of left ventricular activity or both [16]. Nevertheless, these findings suggest that it may be possible to resuscitate more patients with PEA than was previously thought possible. Specifically, these findings are consistent with the clinical data from a concurrent clinical trial demonstrating that in patients with PEA at any time during a resuscitation effort, there was a significant increase in 24-h survival rates in patients treated with the active ITD (27%) when compared with a sham device (11%), most likely because the ITD augments blood pressure in this patient population [15]. Based upon these observations, we speculate further that patients in asystole may benefit from the combination of transthoracic pacing and the ITD, as pacing would provide the cardiac depolarization and the ITD the needed augmentation in venous return, which could consequently result in increased vital organ perfusion and blood pressure.

During the course of this study it was observed that patients were treated with excessive ventilation rates. This finding was the subject of a prior publication [12]. As such, the ITD was modified at the midpoint of the current study. The new ITD (Fig. 1B) has ventilation timing lights to guide ventilation rates. This change was made for both the sham and active ITD so that all EMS personnel who used the ITD would remain blinded to ITD functionality. In addition, towards the

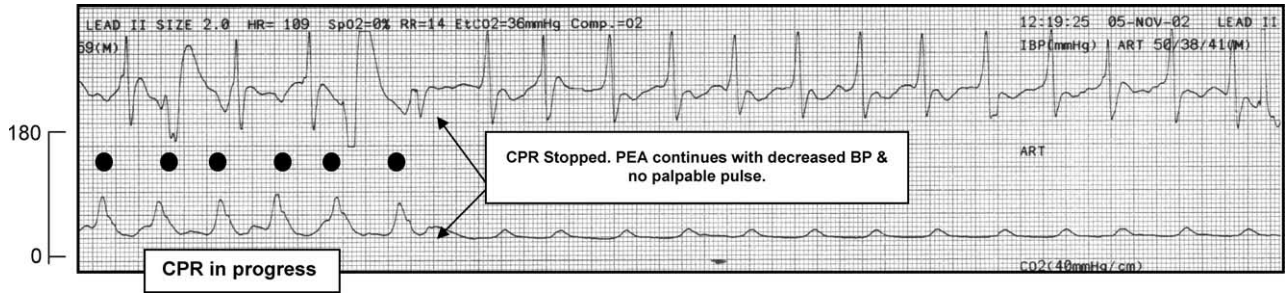


Fig. 3. Example of invasive arterial pressures during PEA with and without CPR. Top channel is the ECG; bottom channel shows invasive arterial pressures; black dots denote chest compressions. In this example, blood pressure is 95/40 mmHg during chest compressions and then decreases to 50/38 when chest compressions are discontinued.

midpoint of the study, the city of Milwaukee initiated a continuous quality improvement program whereby a paramedic monitor was assigned to go to each cardiac arrest during daytime hours to evaluate the quality of CPR performance at the scene. This helped to assure a high quality of conventional CPR during the second half of the study. Analysis of the data from the first half of the study using an ITD without timing lights and data from the second half of the study with devices with timing lights showed that the use of the active ITD resulted in a similar augmentation in blood pressure compared with sham controls. While the sample size was small, analysis of variability between the different halves of the study suggest that use of the ITD with timing lights resulted in less variability in blood pressure in the sham control group. This could be due to several potential causes including use of the timing lights, small sample size with a single patient outlier in one of the subgroups, or the continuous feedback from the paramedic monitor. It is important to note that by the time the hemodynamic measurements were made in this study, the ITD had been attached to the patient's tracheal tube for approximately 14 min, and during that time the personnel providing CPR received regular feedback related to the quality of the CPR they were performing. During the hemodynamic acquisition phase of the study the ventilation rates between the active and sham ITD groups were virtually identical, and ranged between 11 and 14 breaths/patient.

Finally, there were no clinically significant adverse events associated with the use of an active ITD or with the performance of invasive blood pressure monitoring in the field. Oxygen saturation levels were similar between groups, suggesting that, despite the fact that use of the ITD slightly increases dead space ventilation during CPR, it does not adversely affect oxygen delivery. These data are similar to those observed in animals [2–5].

5. Conclusions

The results from this study demonstrate that there was a near doubling of systolic blood pressure when the active ITD was used in patients with an out-of-hospital cardiac arrest. This was associated with a non-significant increase in diastolic blood pressures and $ETCO_2$ and correlated well with a significant increase in short-term survival rates in patients with PEA in a concurrent clinical survival study. As such, we believe that the ITD is a valuable CPR adjunct that can enhance circulation safely and effectively in patients undergoing conventional manual CPR.

Conflict of interest statements

Ronald G. Pirrallo, MD, MHSA: Dr. Pirrallo has served as an ad hoc consultant to ZOLL Medical Inc. and GE/Marquette Electronics Inc., and owns common stock in ZOLL Medical Inc.

Tom Aufderheide, MD: Dr. Aufderheide has served as Basic Life Support Science Editor for the National American Heart Association (paid position). He has received research funding from: (1) GE/Marquette Medical Systems Inc., for a 12-SL Ischemia Project; (2) National Heart, Lung and Blood Institute (NHLBI) SBIR for the current study; (3) NHLBI for the Public Access Defibrillation (PAD-1) Trial, (4) NHLBI for the Resuscitation Outcomes Consortium, and (5) NHLBI for the IMMEDIATE Trial. He is a paid consultant to Medtronic Physio-Control, has served as an ad hoc consultant to GE/Marquette Medical Systems Inc. and ZOLL Medical Inc., and has served in the SBIR study section for the NHLBI.

Keith Lurie, MD: Dr. Lurie is a co-inventor of the impedance threshold device and the active compression–decompression (ACD) CPR device and founded a company, Advanced Circulatory Systems Incorporated (formally CPRx LLC), to further develop this technology.

Terry Provo, BA, EMT-P: Ms. Provo is the Director of Clinical Trials for ACSI.

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