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# Evaluation of an impedance threshold device in patients receiving active compression–decompression cardiopulmonary resuscitation for out of hospital cardiac arrest

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**Abstract**

*Aims:* The purpose of this multicentre clinical randomized controlled blinded prospective trial was to determine whether an inspiratory impedance threshold device (ITD), when used in combination with active compression–decompression (ACD) cardiopulmonary resuscitation (CPR), would improve survival rates in patients with out-of-hospital cardiac arrest. *Methods and results:* Patients were randomized to receive either a sham ($n = 200$) or an active impedance threshold device ($n = 200$) during advanced cardiac life support performed with active compression–decompression cardiopulmonary resuscitation. The primary endpoint of this study was 24 h survival. The 24 h survival rates were 44/200 (22%) with the sham valve and 64/200 (32%) with the active valve ($P = 0.02$). The number of patients who had a return of spontaneous circulation (ROSC), intensive care unit (ICU) admission, and hospital discharge rates was 77 (39%), 57 (29%), and 8 (4%) in the sham valve group versus 96 (48%) ($P = 0.05$), 79 (40%) ($P = 0.02$), and 10 (5%) ($P = 0.6$) in the active valve group. Six out of ten survivors in the active valve group and 1/8 survivors in the sham group had normal neurological function at hospital discharge ($P = 0.1$). *Conclusion:* The use of an impedance valve in patients receiving active compression–decompression cardiopulmonary resuscitation for out-of-hospital cardiac arrest significantly improved 24 h survival rates.


*Keywords:* Cardiac arrest; Active compression–decompression; Cardiopulmonary resuscitation (CPR); Impedance threshold device; Outcome

**Resumo**

*Objectivo:* O objectivo deste estudo clínico multicêntrico prospectivo aleatorizado cegamente controlado foi determinar se um aparelho do limiar de impedância inspiratório (IDT), quando utilizado em combinação com a reanimação cardio-pulmonar (CPR) com Compressão–Descompressão activa (ACD), melhora a taxa de sobrevivência nas vítimas de paragem cardíaca extra-hospitalar. *Método e resultados:* Os doentes foram aleatorizados para receber quer uma simulação ($n = 200$) ou um aparelho do limiar de impedância activo ($n = 200$) durante o suporte avançado de vida realizado com reanimação cardio-pulmonar com compressão-descompressão activa. O primeiro alvo deste estudo foi a sobrevivência às 24 horas. A taxa de sobrevivência às 24 horas foi 44/200 (22%) com a válvula simulada e 64/200 (32%) com a válvula activa ($P = 0.02$). O número de doentes que recuperou a circulação espontânea (ROSC), as admissões na Unidade de Cuidados Intensivos (ICU), e as taxas de alta hospitalar foram 77 (39%), 57 (29%), e 8 (4%) no grupo de simulação versus 96 (48%) ($P = 0.05$), 79 (40%) ($P = 0.02$), e 10 (5%) ($P = 0.6$) no grupo com válvula activa. Seis de dez sobreviventes no grupo válvula activa e 1/8 sobreviventes no grupo simulação tinham uma função neurológica normal na altura da alta hospitalar ($P = 0.1$). *Conclusão:* A utilização de uma válvula de impedância nos

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doentes que recebem reanimação cardio-pulmonar com compressão-descompressão activa para a paragem cardíaca extra-hospitalar melhora de forma significativa a taxa de sobrevivência às 24 horas.


*Palavras chave:* Paragem cardíaca; Compresão-descompressão activa; Reanimação cardio-pulmonar (CPR); Válvula do limiar de impedância; Prognóstico

**Resumen**

*Objetivo:* El propósito de este estudio clínico prospectivo, randomizado, multicéntrico ciego controlado fue determinar si un dispositivo de umbral de impedancia inspiratoria (ITD), usado en combinación con reanimación cardiopulmonar (CPR) con compresión y descompresión activa (ACD), mejoraría las tasas de sobrevida en pacientes con paro cardiorespiratorio extrahospitalario(OHCA). *Métodos y Resultados:* Los pacientes fueron randomizados para recibir un dispositivo simulado($n = 200$) o un dispositivo de impedancia activa ($n = 200$) durante el soporte vital avanzado realizado con CPR de ACD. La meta primaria de este estudio fue la sobrevida a las 24 horas. Las tasas de sobrevida a las 24 hrs fueron 44/200 (22%) con la válvula simulada y 64/200 (32%) con la válvula activa ($P = 0.02$). El número de pacientes que tuvieron retorno a circulación espontánea (ROSC), admisión a unidad de cuidados intensivos (ICU), y tasas de alta hospitalaria fue de 77 (39%), 57 (29%), y 8 (4%) en el grupo simulado versus 96 (48%) ($P = 0.05$), 79 (40%) ($P = 0.02$), y 10 (5%) ($P = 0.6$) en el grupo de la válvula activa. 6 de 10 sobrevivientes en el grupo de válvula activa y 1 de 8 de los sobrevivientes del grupo simulado tenían función neurológica normal al alta hospitalaria ($P = 0.1$). *Conclusión:* El uso de una válvula de impedancia en pacientes que reciben CPR ACD para paro cardiaco extrahospitalario mejoró significativamente las tasas de sobrevida a las 24 horas.


*Palabras clave:* Paro cardíaco; Compresión-descompresión activa; Reanimación cardiopulmonar (RCP); Válvula de umbral de impedancia; Resultado

## 1. Introduction

Most people die from cardiac arrest, despite receiving cardiopulmonary resuscitation (CPR). There are many reasons for the high mortality rates, notably the time to the start of CPR, and the inherent inefficiency of CPR itself. While time to initiation of CPR is dependant upon the overall efficiency of the emergency medical services, standard manual CPR is intrinsically inefficient as the chest compression promotes forward flow but there is little to promote the return of blood back into the heart. Indeed, standard CPR only provides 10–20% of normal blood flow to the heart and 20–30% of normal blood flow to the brain [1–3]. Many have tried to develop new CPR techniques [4–9]. Most efforts have focused on means to increase systemic pressures directly during the compression phase of CPR. Two approaches have been recently discovered to increase venous return to the heart during the decompression phase, thereby priming the pump for each subsequent compression phase.

The first one is active compression–decompression (ACD) CPR [10–13]. It is performed with a hand-held suction device fixed on the anterior chest wall. During the compression phase, the chest is compressed and blood is forced out of the heart to perfuse the vital organs. When actively pulling up with the device, a vacuum is created within the thorax, drawing more blood back into the heart. This technique is known to improve haemodynamics [3,10] and, in some studies, survival rates in patients in cardiac arrest compared with patients receiving standard CPR [12,13]. A second approach involves use of the impedance threshold device (ITD) during CPR [14–16]. It is a small (35 ml) valve with a silicone diaphragm that can be attached to the tracheal tube or face mask or laryngeal mask airway [16,17] (see Fig. 1). When not actively ventilating the patient, the diaphragm is designed to selectively impede inspiratory airflow into the patient when the intrathoracic pressure is less than 0 atm, thereby increasing the degree of negative intrathoracic pressure with each chest decompression when compared with CPR alone. This creates and maintains a vacuum within the chest to improve venous return back to the heart further. During active ventilation by the rescuer, neither inspiratory

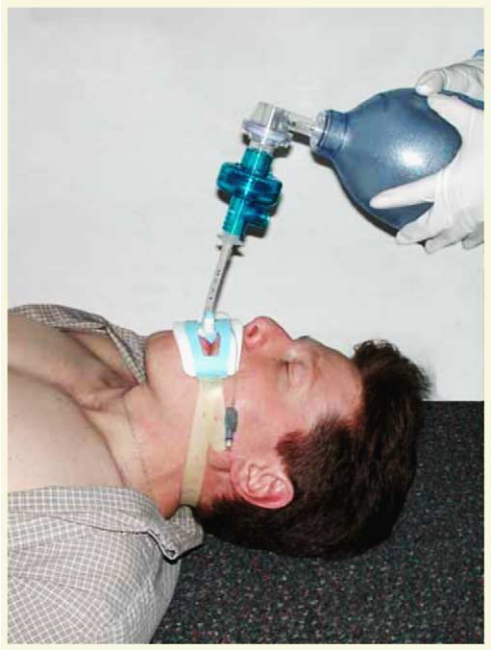

Fig. 1. Figure demonstrates the use of ITD with a resuscitator bag. The ITD was colored blue to prevent the user from knowing if it was active or sham.

nor expiratory gas exchange to the patient is impeded by the ITD. Similarly, with chest compression, there is no resistance to the movement of air out of the chest [15]. Should the patient gasp spontaneously, or begin to breathe on his or her own, then ventilation is possible through a side port safety check valve set to open at −21 cm $H_2O$. The ITD is removed after there is a return of spontaneous circulation (ROSC).

Recently, animal studies have demonstrated that ITD improves vital organ blood flow and survival rate during standard and, to a greater degree, during ACD CPR because of the enhancement of the decrease in intrathoracic pressure with active chest wall decompression [1,18–20]. Based upon the improvement in blood pressure and coronary perfusion pressure in patients treated with the combination of the ACD CPR and ITD [14], this device combination was given a Class IIb recommendation in the International CPR Guidelines 2000 (“acceptable alternative” to standard CPR) [21,22].

Based upon these promising results, the present study was designed to determine if the combination of ACD CPR with the ITD would result in improved short-term survival rates when compared with ACD CPR alone.

## 2. Material and methods

This prospective multi-site clinical randomized blinded trial complies with the Declaration of Helsinki. It was approved by the Consultative Council for the Protection of Persons Volunteering for Biomedical Research of Lariboisière Saint-Louis University, Paris. This ethical committee waived the requirement for informed consent since it was not possible under the clinical circumstances and the committee felt that the study was justified based upon a previous haemodynamic study with the same devices [14].

The study was performed in northern Paris metro areas, Vernon, Gisors, Lyon, and Thionville. A two-tiered response system is responsible for answering all emergency calls in these EMS systems [13]. Patient enrollment began in September 1999 and ended in August 2000. In these study sites, the first-tier response is made by fire rescue personnel. They were equipped with basic life support (BLS) equipment and automatic external defibrillators. They all practiced basic CPR systematically with the ACD as the primary initial resuscitation technique. The second-tier response provided advanced care. This was a physician-based and led response team. They provided advanced airway support, advanced life support (ALS) with pharmacological therapy and manual defibrillation. As usually practiced, BLS, and ALS were both performed on the scene until the patients were successfully resuscitated or if the physician decided to stop the manoeuvers except for specific cases i.e. profound hypothermia. Resuscitated patients were directly transported by the medical team to an intensive care unit (ICU).

Patients older than 18 years of age with an out-of-hospital cardiac arrest were enrolled in the study. Adhering to standard operating clinical protocols, no patient received CPR from the advanced life support team who had presumed irreversible death, known terminal illness, traumatic injuries, those who had made “do not resuscitate” orders, those in whom the known time from cardiac arrest to start of basic CPR exceeded 30 min and those in whom a spontaneous palpable carotid or femoral pulse was restored before the arrival of the medical team. Patients meeting these criteria were excluded from the study.

The personnel had been previously trained in ACD CPR and, for the purposes of this study, no additional ACD CPR training was provided. There was no specific training associated with the use of the ITD, with the exception that co-investigators were instructed to attach the ITD to the tracheal tube and remove it as soon as there was a return of spontaneous circulation. During BLS, ventilation was performed using manual bag/valve/mask ventilation with 100% oxygen and a ventilation/compression ratio of 2:15.

Upon the arrival of the ALS team, patients were randomized to receive either ACD CPR with an active ITD or ACD CPR with a sham valve. The active impedance valves (CPRx LLC, Minneapolis, Minnesota) were designed to prevent airflow into the patient during chest wall decompression. If the negative pressure within the thorax reached a value of more than −21 cm $H_2O$, the valve would open allowing inflow of oxygen. Specifically for this study, sham valves were created by the manufacturer (CPRx LLC, Minneapolis, Minnesota) by removing the silicone diaphragm and by occluding the diaphragm venting ports. As such, the sham valves functioned as hollow conduits. Furthermore, all the valves were colored dark blue so that the rescuers could not determine whether or not the silicone diaphragm was present. All valves were labeled with a serial number and a code. Each site received at least one box of 10 valves. Half of them were sham valves and the other one-half were active valves. The randomization code was held by an independent statistician (E.V.) and this remained unknown to all investigators until after study enrollment was completed. Investigators were instructed to use the valves sequentially for each patient in cardiac arrest who required on-going CPR with ALS.

Once intubated, the valves were inserted between the tracheal tube and the inspiratory circuit and they continued to receive ACD CPR for a minimum of 30 min by the ALS team and the first response team. Chest compressions were performed at a frequency of 100 $min^{-1}$ with the aid of a metronome. Ventilation was performed asynchronously by means of an automatic pressure cycle portable ventilator (Airox, Bio MS, Pau, France) at a rate of 10 $min^{-1}$, a tidal volume of 8 ml/kg of body weight and an inspired oxygen fraction of 100%. This is part of the routine care for patients undergoing CPR in France. The teams rotated performance of ACD CPR every 3–5 min to prevent fatigue [13]. Low

dose adrenaline (epinephrine) (1 mg) was administered every 3–5 min according to international guidelines [21,22]. After successful resuscitation the valve was removed from the circuit.

We followed the Utstein Template Guidelines for data collection [23]. Data collection forms were completed for each patient. There were no deviations from the routine care provided to patients in the study sites, with the exception that either a sham or active valve was used.

The primary endpoint of this study was 24 h survival. Secondary endpoints included the rate of return of spontaneous circulation, intensive care unit admission rates, hospital discharge rates, neurological scores at the time of hospital discharge, as determined by the cerebral performance score (Glasgow–Pittsburgh cerebral performance category (CPC) neurological scoring systems) [23] and the complication and adverse event rates. Data were also analyzed based upon the initial rhythm that was observed and whether or not the arrests were witnessed.

Data were analyzed on an intention to treat basis. Sample size was determined on the following bases: we estimated that the percentage of patients surviving after 24 h in the sham valve group will be close to 20% and we calculated that $n = 200$ patients per group will allow a 80% power to detect a 12% difference in the percentage of patients surviving after 24 h corresponding to an OR = 1.9 using a chi-square test with a two-sided significance level fixed at 5%. Chi-square test and 95% confidence intervals (CI) were used for analysis of the primary and secondary endpoints. When conditions of validity of chi-square or for asymptotic method for calculation of CI were not fulfilled, Fisher's exact probability test and exact CI were used. All tests were made using StatXact (from cytel Software Cambridge MA, USA). A $P$ value of $<0.05$ was considered statistically significant.

## 3. Results

A total of 618 emergency calls for cardiac arrests were recorded during the study period. Of these, 218 patients were excluded from enrollment and did not receive ALS. BLS was not provided in 57 patients because of irreversible death and in three patients with do-not-resuscitate orders. ALS was not provided in 56 patients with a terminal illness and in the 69 patients with a known time from collapse to initiation of basic CPR greater than 30 min. A total of 33 patients recovered following BLS and early defibrillation, before the arrival of the medical team. The remaining 400 patients were randomized in this clinical trial: 200 received a sham valve and 200 received an active valve. The clinical characteristics of the patients, the essential time intervals during the resuscitation effort, and the dose of adrenaline used during CPR are shown in Table 1. The groups were similar in all categories.

Table 1
Patient characteristics

| Variable | ACD CPR + sham ITD ($n = 200$) | ACD CPR + active ITD ($n = 200$) |
|---|---|---|
| Age ± S.E.M (years) | 60 ± 1.3 | 58 ± 1.3 |
| Gender (%) | | |
| Male | 66.5 | 66.5 |
| Female | 33.5 | 33.5 |
| Arrest witnessed (%) | 75 | 74 |
| Bystander CPR (%) | 10 | 9.5 |
| Response intervals (min ± S.E.M) | | |
| call to BLS arrival | 8.8 ± 0.5 | 8.4 ± 0.4 |
| call to MICU arrival | 18.5 ± 0.7 | 17.4 ± 0.7 |
| Initial rhythm (%) | | |
| V-fib/pulseless V-tach | 23 | 26 |
| PEA | 2.5 | 5 |
| Asystole | 74.5 | 69 |
| Arrest site (%) | | |
| Home | 64 | 69 |
| Public place | 12.5 | 11.5 |
| Street | 14.5 | 12.5 |
| Work place | 2.5 | 1 |
| Medical environment | 6.5 | 6 |
| CPR duration[a] (min ± S.E.M) | 27.0 ± 1.03 | 29.1 ± 1.39 |
| Total Adr administered[a] (mg ± S.E.M) | 9.2 ± 0.4 | 10.0 ± 0.5 |

ACD, active compression–decompression; CPR, cardiopulmonary resuscitation; ITD, impedance threshold device; Adr, adrenaline (epinephrine); BLS, basic life support; ALS, advanced life support; PEA, pulseless electrical activity; V-fib, ventricular fibrillation; V-tach, ventricular tachycardia; SEM, standard error of the mean.

[a] In those patients not achieving return of spontaneous circulation.

The rates of ROSC, ICU admission, 24 h survival, hospital discharge and neurological scores at hospital discharge are shown for all patients in Table 2. There was a statistically significant increase in 24 h survival in patients treated with the active ITD. In addition, we observed a significant increase in ICU admission rates. All patients discharged from the hospital had a CPC score of either 1 or 2. Normal neurological function (CPC = 1) was observed in 6/10 survivors treated with the active valve and 1/8 survivors treated with a sham valve ($P$ = NS).

A total of 46 patients in the active valve group and 52 patients in the sham valve group had an initial rhythm of ventricular fibrillation. The 24 h survival rates were 54% in the active valve group and 40% in the sham valve group (NS). Only five patients survived with ventricular fibrillation in each group to hospital discharge. Neurological function was normal in 4/5 patients in the active valve group and 1/5 patients in the control group ($P$ = NS).

As shown in Table 3, the frequency rate of rib fractures, sternal fractures, and pulmonary edema were compared between groups. There were no adverse events associated with the use of the active valve.

Table 2
Clinical outcomes

| Outcome | All patients: sham valve ($n = 200$) | All patients: active valve ($n = 200$) | All patients OR (95% CI) | Witnessed patients: sham valve ($n = 148$) | Witnessed patients: active valve ($n = 150$) | Witnessed patients: OR (95% CI) |
|---|---|---|---|---|---|---|
| ROSC, *n* (%) | 77 (38.5) | 96 (48) | 1.48 [0.99–2.19] $P = 0.056$ | 72 (48.7) | 84 (56) | 1.34 [0.85–2.19] $P = 0.2$ |
| ICU admission, *n* (%) | 57 (28.5) | 79 (39.5) | 1.64 [1.08–2.49] $P = 0.02$ | 54 (36.5) | 72 (48) | 1.60 [1.01–2.55] $P = 0.04$ |
| >24 h survival *n* (%) | 44 (22) | 64 (32) | 1.67 [1.07–2.6] $P = 0.02$ | 41 (27.7) | 58 (38.7) | 1.64 [1.01–2.68] $P = 0.045$ |
| Hospital discharge *n* (%) | 8 (4) | 10 (5) | 1.26 [0.49–3.27] $P = 0.63$ | 8 (5.4) | 10 (6.7) | 1.25 [0.48–3.26] $P = 0.65$ |
| Neuro function: | | | | | | |
| CPC = 1 | 1 | 6 | 10.5 [0.7–550.2] $P = 0.11$ | 1 | 6 | 15 [0.7–824] $P = 0.10$ |
| CPC = 2 | 7 | 4 | | 7 | 4 | |

Neuro, neurological; CPC, Cerebral performance category (CPC of 1 is normal cerebral function); ROSC, return of spontaneous circulation; CI, confidence interval; OR, odds ratio; ICU, intensive care unit.

Table 3
Complications

| Complications, *n* (%) | ACD CPR + sham valve ($n = 200$) | ACD CPR + active valve ($n = 200$) | *P* value |
|---|---|---|---|
| Rib Fractures | 60 (30) | 78 (39) | 0.06 |
| Sternal Fractures | 12 (6) | 5 (2.5) | 0.13 |
| Pulmonary edema | 14 (7) | 8 (4) | 0.27 |

ACD, active compression–decompression; CPR, cardiopulmonary resuscitation.

## 4. Discussion

The combination of ACD CPR with the ITD has been shown recently to improve coronary artery perfusion pressures and systemic blood pressures significantly in animals and patients in cardiac arrest when compared with ACD CPR alone [14,16]. Results from the present study confirm that the haemodynamic benefit observed in previous studies translates to a direct increase in survival rates and improved neurological function. In the current study, the principal endpoint was 24 h survival. We observed a nearly 50% increase in 24 h survival for patients treated with ACD CPR and an active valve when compared with the sham valve. Both the ACD CPR device and the ITD were designed to enhance vital organ circulation by enhancing venous return during CPR. This is the first report of any human survival data comparing ACD CPR plus the ITD to ACD CPR alone. While this initial study was not designed or statistically powered to determine if the new device combination could increase hospital discharge rates or improve neurological outcome, use of the ITD was associated with normal neurological function in 6/10 patients at hospital discharge versus 1/8 patients in the sham valve control group.

ACD CPR has been studied and found to improve circulation during cardiac arrest and, in some clinical trials, to improve short and long-term outcomes. However, the combination of ACD with the ITD optimizes the bellows action of the thorax during CPR and increases cardiopulmonary circulation by enhancing venous return during the decompression phase and then by augmenting systemic pressure during the compression phase. The observed benefits of the combination of ACD CPR with the ITD demonstrate that survival rates after cardiac arrest can be significantly improved by enhancing fundamental physiological processes during resuscitation. These findings are consistent with the hypothesis that “priming the pump” is critical for survival after cardiac arrest [24]. These findings are also consistent with a recent prehospital clinical trial in Germany where 24 h survival rates were found to be significantly improved with the combination of ACD CPR and the ITD when compared with standard CPR alone (37% versus 22%; $P = 0.03$) [25]. The present results show that the ITD component of this combination is beneficial. Because of its simplicity to be taught and used, one could imagine that this device can be sufficient to enhance venous return in cardiac arrest patients as already demonstrated in animals [20]. Nevertheless, if the ITD is used with standard manual CPR, the rescuers must allow the chest to fully recoil after each compression in order to optimize the benefit of the ITD. One advantage of the ITD + ACD combination is that the ACD component helps to assure that the intrathoracic pressure will become more negative (depth and duration) during the chest wall decompression phase. In addition, correct use of the combination of ITD + ACD devices causes a more rapid decrease in negative intrathoracic pressure than either device alone. This contributes to a greater influx of venous blood back to the heart with each decompression phase.

Unlike other CPR device studies, which are nearly impossible to perform in a blinded fashion, the current study was performed in a prospective randomized blinded trial, by developing a sealed disposable sham valve that looked identical to the active valve. Furthermore, when performing compressions and decompressions, there was no special sound coming from the active valves that could offer the rescuer any audible distinction from the sham valves. In

addition, we intentionally did not try to retrain rescuers in the performance of ACD CPR specially for the study because they had used this technique as standard practice for a long time, were trained regularly, and teams were always supervised by a physician at the scene. The actual purpose of the study was to see what impact the impedance valve may have in the "real world" when added to the care of patients in our EMS systems. However, in the present study, it is important to note that the survival rates with ACD alone (used as a standard technique) were similar to those seen in our previous studies when used as a study technique [12,13].

Based upon previous studies [12–14], patients in the current evaluation received at least 30 min of ACD CPR after undergoing tracheal intubation. This duration of CPR is important and in this study was sufficient to "prime the pump" to optimize venous return. As in previous studies [12,13], most of the patients in the current study were in asystole or had pulseless electrical activity when the first rhythm was recorded. This high incidence of non ventricular fibrillation rhythms may be due, at least in part, to the long intervention times for the first-tier ambulance (>8 min) and for the medical team (>17 min). Nevertheless, it has been shown in previous studies that, regardless of the presenting rhythm, the use of ACD CPR or ACD + ITD CPR can increase short-term outcomes, respectively [11–15,25]. In the study by Wolcke et al., ACD + ITD CPR extended the "window of opportunity" for successful resuscitation by enhancing circulation.

This study is limited in that the primary endpoint for this first clinical trial was 24 h survival. Based upon the findings in this study, we estimate that a definitive trial demonstrating improved survival to hospital discharge rates would require approximately 400 patients per treatment arm. Despite the lack of a longer term endpoint, we believe that the increase in 24 h survival rates represents a clinically meaningful improvement in patient care. We believe that survival to 24 h may be an even more important surrogate for a successful long term benefit than other outcome measures such as return of spontaneous circulation or hospital admission rate, commonly used to evaluate new therapies such as amiodarone [26], or termination of ventricular fibrillation, and the evaluation of new defibrillation waveforms [27]. The study is also limited in that we applied the ITD late in the sequence of CPR, thereby potentially underestimating its impact. In this regard, recent studies have shown that the ITD can be connected to either a tracheal tube or a face mask and result in a significant reduction in intrathoracic pressure when compared to a sham valve alone [17]. Taken together, these studies suggest that early use of ACD CPR with the ITD is feasible for deployment with first-tier responders. Another limitation is that the frequency of asystole is high in the current study but similar to that which we have reported previously [12,13]. This may prevent a generalized interpretation of the results, or potentially underestimate the impact of the impedance valve. The study from Wolcke et al. confirms this fact, while the use of ACD + ITD significantly increased short-term survival in patients victims of out-of-hospital ventricular fibrillation compared to standard manual CPR [25]. Finally, we were unable to perform autopsies or determine whether the addition of the impedance valve altered gas exchange. Other studies should be performed to address more precisely the problem of complications when using the ITD.

## 5. Conclusions

While rapid deployment of emergency response personnel is a key element to successful resuscitation, the advances made in circulation to the vital organs with the combination of ACD CPR and the ITD have been shown, for the first time in the current study, to translate directly into improvement in overall short-term survival rates when compared with ACD CPR alone. Brain function was at least as good in the survivors with the new technique compared with controls. Building upon the positive short-term survival rates and the overall effect size observed in the present study, a larger clinical trial designed to determine the potential long term benefit of this technology can now be initiated.

## Conflict of Interest

The authors confirm that all authors participated in this study and all have seen and agree with the results in the final manuscript. Regarding conflict of interests, Dr. Lurie is a co-inventor of the impedance threshold device and active compression decompression device and founded a company, CPRx LLC, to further develop this technology. All the other authors did not have any conflict of interest within 3 years of beginning the work submitted.

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