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EDITORIAL

Use of the impedance threshold device in cardiopulmonary resuscitation

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Abstract

Although approximately one million sudden cardiac deaths occur yearly in the US and Europe, cardiac arrest (CA) remains a clinical condition still characterized by a poor prognosis. In an effort to improve the cardiopulmonary resuscitation (CPR) technique, the 2005 American Heart Association (AHA) Guidelines for CPR gave the impedance threshold device (ITD) a Class IIa recommendation. The AHA recommendation means that there is strong evidence to demonstrate that ITD enhances circulation, improves hemodynamics and increases the likelihood of resuscitation in patients in CA. During standard CPR, venous blood return to the heart relies on the natural elastic recoil of the chest which creates a transient decrease in intrathoracic pressure. The ITD further decreases intrathoracic pressure by preventing respiratory gases from entering the lungs during the decompression phase of CPR. Thus, although ITD is placed into the respiratory circuit it works as a circulatory enhancer device that provides its therapeutic benefit with each chest decompression. The ease of use of this device, its ability to be incorporated into a mask and other airway devices, the absence of device-related adverse effects and few requirements in additional training, suggest that ITD may be a favorable new device for improving CPR efficiency. Since the literature is short of studies with clinically meaningful outcomes such as neurological outcome and long term survival, further evidence is still needed.

Key words: Cardiopulmonary resuscitation; Coronary perfusion pressure; Impedance threshold device; Return of spontaneous circulation; Survival

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INTRODUCTION

Although the term cardiopulmonary resuscitation (CPR) was first published 50 years ago, the origins of resus-

citation extend back centuries. Various methods of resuscitation have been used throughout the ages with the oldest example from around 3000 BC, being the introduction of smoke into the rectum as depicted in hieroglyphics and cave drawings of the Mayan and Inca people of South and Central America. The first apparent attempt of resuscitation was recorded in the Bible around 800 BC and was Elijah's mouth to mouth ventilation[1].

Very early in our history, people realized that the body became cold when lifeless, and therefore connected heat with life. In order to prevent death, the body was warmed. The use of warm ashes, burning excrement, or hot water placed directly on the body were all employed in an attempt to restore life[2].

The first report of an experimental intubation of the trachea was probably by the great Muslim philosopher and physician Avicenna around the year 1000[3]. "When necessary, a cannula of gold, silver or another suitable material is advanced down the throat to support inspiration." In 1543, Vesalius *et al*[4] published "De humani corporis fabrica" which described blowing into a tube to resuscitate an animal.

During Enlightenment, starting around 1750, Goodwin and Kite hypothesized that asphyxia causes the heart to stop. Kite suggested electric shock treatment (defibrillation), but airway problems produced by the tongue were not appreciated at that time[5]. Marshall Hall was the first to realize that leaving the victim supine allows the tongue to fall backwards blocking the airway and he supported the notion that the prone position should be employed in resuscitation[6].

In the year 1957, Dr. Peter Safar, in a series of elegant and daring experiments on curarized volunteers, showed that tilting the head could open the airway and that the mouth-to-mouth technique of artificial ventilation was superior over all others techniques described before[7,8]. Three years later Kouwenhoven *et al*[9] published a paper on closed-chest cardiac "massage", after observing that chest compressions produced arterial pulses. They confirmed the usefulness of chest compressions by performing experiments with anesthesia-induced cardiac arrests.

Modern published studies report that about one million people suffer cardiac arrest (CA) each year in the United States and Europe, almost one every 30 s. Many of them will undergo CPR by bystanders and emergency medical services (EMS) in a desperate attempt to restore life. Unfortunately, according to recent literature, only 1 in 5 adults survive in-hospital CA while less than 1 in 10 adults survive out-of-hospital CA[10-13]. These statistics are somewhat sobering, especially when compared with survival rates of the first resuscitative techniques ever developed and reported[14].

In addition, recent statistics on neurological recovery after resuscitation are also disappointing when put into historical perspective. Stephenson *et al*[14] reported that 56% of the 1200 CA victims were successfully resuscitated, and only 8 of these patients were rendered decerebrate. Furthermore, the first successful human defibrillation, in 1947, involved CPR for over an hour, and yet the patient had no long-term neurological deficits[15]. Neurological injury after resuscitation of a witnessed CA victim means that CPR efforts failed to provide sufficient cerebral blood flow. Needless to say, novel CPR techniques should achieve not only cardiopulmonary but also neurological recovery.

A number of new mechanical devices have been developed in recent years to improve the present dismal outcomes for patients in CA[16]. The 2005 American Heart Association (AHA) guidelines gave the impedance threshold device (ITD) a Class IIa recommendation[17]. The AHA recommendation means that there is strong evidence to demonstrate that the ITD (Figure 1) enhances circulation, improves hemodynamics and increases the likelihood of resuscitation of CA victims. It is the most highly recommended CPR adjunct and carries a higher recommendation than any medication used in adult CPR.

CORONARY PERFUSION PRESSURE AND BLOOD FLOW

Various studies have shown that coronary perfusion pressure (CPP), generated during CPR, is the only key component for successful resuscitation. CPP is the pressure gradient between the ascending aorta and the right atrium during the "diastolic" or decompression phase of CPR. Like the physiology of normal sinus rhythm, myocardial blood flow occurs only during the artificial diastole or the chest relaxation phase of CPR. An increased right atrial pressure may impede venous return of myocardial blood flow to the right atrium. This impeding pressure must be subtracted from the driving pressure (aortic diastolic pressure) to calculate the perfusion pressure gradient[18].

CPP has been correlated with myocardial blood flow generated during CPR and both successful resuscitation and return of spontaneous circulation (ROSC)[19-21]. Kitakaze *et al*[22] clearly shows that successful resuscitation is correlated with both the CPP produced and the resultant left ventricular myocardial blood flow. Furthermore, CPP has been associated with longer-term outcomes including from 1 to 24-h survival and even 7-d survival[23-25].

PHYSIOLOGY OF CPR

The objective of any CPR effort is to pump blood from the heart to the vital organs with each chest compression and to enhance the return of blood back to the heart with each chest relaxation. Two different theories attempt to explain the mechanism of blood flow during CPR[26].

The "cardiac pump theory" is based on the concept that the heart is compressed between the spinal column and the sternum during chest compressions[27]. This theory requires that the atrioventricular valves be closed during cardiac compression (systole).

Figure 1 The impedance threshold device.

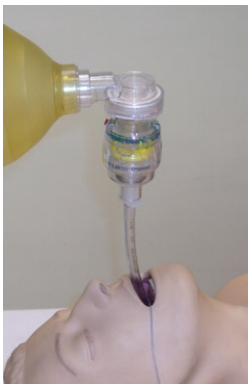

Figure 2 The impedance threshold device attached to the endotracheal tube of an intubated manikin.

On the other hand, in the "thoracic pump theory", external pressure on the chest causes an increase in intrathoracic pressure without direct compression of the heart with the latter acting as a passive conduit[28]. This theory requires that the atrioventricular valves be open during cardiac compression. The increase in intrathoracic pressure is evenly distributed over all heart chambers and intrathoracic vascular structures. Therefore, a pressure gradient towards the aorta is generated, resulting in forward blood flow. In fact, during the compression phase of CPR the intrathoracic pressure rises from 5-25 mmHg. This positive pressure forces blood out of the heart to vital organs. However, the compression phase is only half of the duty cycle. During chest wall relaxation, intrathoracic pressure falls to approximately -5 mmHg[29]. This decrease in intrathoracic pressure to sub-atmospheric levels creates a vacuum relative to the rest of the body, sufficient to propel some movement of venous blood from the periphery back into the right heart. This is a very critical phase because if the heart is not filled with blood there would not be sufficient blood circulated forward in the next chest compression. It is also during the decompression phase that the coronary arteries supply the heart muscle with blood[30].

Furthermore, with each chest compression the respiratory gases are actively pushed out of the thorax. On the other hand, during the decompression phase the intrathoracic vacuum works like suction and draws not only blood back into the heart, but also some air back into the lungs. Unfortunately, much of the potential hemodynamic benefit of this vacuum is lost due to the influx of inspiratory gases. Moreover, each time the chest wall recoils a transient decrease in intracranial pressure occurs[31-33].

ITD

Clinically, venous blood flow is increased by the Mueller maneuver, a technique in which inspiration is performed when the trachea is simultaneously occluded by the epiglottis[34]. It is this principle that is further exploited by the ITD in an attempt to further decrease intrathoracic pressure and thus enhance venous return in CPR. The ITD is a small (35 mL), single use, disposable plastic valve that can be attached to a tracheal tube (Figure 2), a face mask, a laryngeal mask or any other protective airway device and must be placed at the respiratory circuit as soon as it becomes available. It has been demonstrated that its effectiveness is the same whether it is used with a face mask or an endotracheal tube[35]. It contains a silicon diaphragm designed to selectively impede inspiratory airflow into the patient when the intrathoracic pressure is less than 0 atm. Hence, as soon as the chest wall recoils back to its resting position the diaphragm occludes the lumen within the valve, preventing all unnecessary air from entering the chest when the patient is not being actively ventilated. This creates and maintains a vacuum within the chest that further improves venous return back into the heart. The maximum negative intrathoracic pressure generated in animal studies ranged from -4 to -8 mmHg while in an intubated patient was -13[36-38]. Without the ITD, intrathoracic pressure was only -3 mmHg[38]. It takes as many as 5 compression/decompression cycles to achieve the maximum negative intrathoracic pressure. Thus, despite its placement into the ventilation circuit, the ITD is a circulatory enhancer device that provides its therapeutic benefit with each chest decompression.

During active ventilation by the rescuer, the lumen within the ITD remains open and there is no resistance to ventilation. Similarly, with chest compression, there is no resistance to the movement of air out of the chest[39]. Spontaneous inspiration through the ITD is possible but may be difficult for a recently resuscitated patient. Cracking pressure, which is the inspiratory pressure necessary to open the valve and allow for spontaneous inspiration within the device, can vary at the time of manufacture. Clinical trials to date have been performed with ITD cracking pressures between -15 cm and -24 cm H_2O[40]. This cracking pressure could increase substantially the work of breathing in a spontaneously breathing subject and it is therefore recommended that the device be removed as soon as subjects start breathing spontaneously.

Furthermore, ResQPOD (newer model ITD) has 2 ventilation timing assist lights on its upper surface. They provide guidance on the correct ventilation rate, when a secured airway has been placed, by flashing 12 times a minute. This visual aid works to avoid hyperventilation given that increased ventilation rates during CPR affect

venous return to the heart, resulting in reduced aortic blood pressure and coronary perfusion pressure[31,32]. Moreover, each time active positive-pressure ventilation is delivered, the decompression phase intrathoracic vacuum is destroyed and requires regeneration[40]. Thus, the less frequent the ventilation rate, the greater the blood flow back to the heart. The ResQPOD's inspiratory impedance feature is independent of the timing lights and inspiratory impedance is provided whether the lights are ON or OFF.

ANIMAL STUDIES

The ResQPOD has been the subject of over 30 clinical trials and animal studies. The first experiments designed to test the impedance valve concept were performed in a pig model of CA.

Standard CPR combined with an ITD

In a study by Lurie *et al*[41], 22 pigs were left untreated for 6 min after induction of ventricular fibrillation. CPR efforts were then performed with either standard CPR plus a sham valve (n = 11) or standard CPR plus a functional valve (n = 11). Use of the functional ITD during standard CPR significantly improved vital organ blood flow and total left ventricular blood flow. Moreover, CPP and cerebral blood flow were higher in the animals treated with the functional valve. An interesting protocol was one in which the ITD was added or removed in a sequential manner in the same animal during the performance of CPR[29]. Authors determined myocardial and brain blood flows with radiolabeled microspheres, while CPP was defined as the aortic-to-right atrial pressure gradient during the relaxation phase of CPR. Each time the ITD was removed from the respiratory circuit, the CPP and vital organ perfusion decreased while perfusion pressures stabilized or increased when the valve was placed back in the circuit. A subsequent prospective, blinded study demonstrated a significantly higher end tidal CO_2 and systolic blood pressure when an active ITD was used[42]. These results were further confirmed by an independent study (without the patent holder as one of the authors) which demonstrated that the ITD doubled blood flow to the heart when compared with standard CPR[43]. Table 1 shows changes in CPP values when ITD was added to CPR efforts.

In addition to an increase in hemodynamics, the beneficial effects of standard CPR plus an ITD can also be seen on survival and neurological function. A statistically significant increase in 24-h survival and neurological function was demonstrated when the ITD was used during standard CPR[42]. One of eleven animals *vs* twelve of seventeen had completely normal neurological function when a sham *vs* an active ITD was used ($P < 0.05$). In addition, the ITD lowers intracranial pressure during the decompression phase similar to the mechanism of the "last gasp", thereby reducing resistance to forward blood flow to the brain[48]. Moreover, Yannopoulos *et al*[49] reported a significant and dose-dependent decrease in intracranial pressure both at baseline and after a successful resuscitation with the use of an ITD compared with spontaneous breathing.

Table 1 CPP values in diverse animal studies

First author	CPR method	CPP	↑ CPP (%) with ITD	*P*-values
Lurie *et al*[36]	ACD-CPR	21 ± 3.6	47.6	< 0.05
	ACD-CPR + ITD	31 ± 2.3		
Lurie *et al*[41]	S-CPR	14 ± 2	42.9	< 0.006
	S-CPR + ITD	20 ± 2		
Raedler *et al*[44]	S-CPR	15 ± 2	93.3	< 0.001
	ACD-CPR + ITD	29 ± 3		
Srinivasan *et al*[45]	S-CPR	17.4 ± 3	64.7	< 0.01
	ACD-CPR + ITD	28.3 ± 2		
Metzger *et al*[46]	S-CPR	22.4 ± 1.6	31.8	< 0.05
	ACD-CPR + ITD	29.5 ± 2.7		
Yannopoulos *et al*[47]	S-CPR	14 ± 3	128.6	< 0.01
	ACD-CPR + ITD	32 ± 5		

CPP: Coronary perfusion pressure; ITD: Impedance threshold device; CPR: Cardiopulmonary resuscitation; ACD-CPR: Active compression decompression cardiopulmonary resuscitation; S-CPR: Standard cardiopulmonary resuscitation.

Active compression decompression CPR (ACD-CPR) combined with an ITD

Various studies combined ITD with an automated device that actively compresses and then decompresses the chest with a suction cup attached to the anterior chest wall.

The addition of an ITD during ACD-CPR in a porcine model of CA resulted in a marked enhancement of vital organ blood flow and coronary perfusion pressure (Table 1) and a decrease in the total energy required for effective defibrillation[36]. A remarkable increase in perfusion pressures and, subsequently, vital organ blood flow above the threshold that rendered successful defibrillation was also demonstrated by Voelckel *et al*[50]. The increase in perfusion pressures and vital organ blood flow occurred when global ischemia reached a point that renders many CPR interventions barely effective. With the use of the ITD, six of seven animals had ROSC after a total of 26 min.

During the very special situation of hypothermic CA, ACD-CPR together with an ITD improved common carotid blood flow compared with standard CPR alone (67 ± 13 mL/min *vs* 26 ± 5 mL/min, respectively, $P < 0.025$)[44]. The beneficial effects of the combination of ACD-CPR with an ITD were also seen on cerebral metabolism. Using the technique of microdialysis, researchers measured the changes in brain biochemistry during and after hypothermic cardiopulmonary arrest. Apparently, ITD improved the lactate-pyruvate ratio and glucose metabolism in comparison to standard CPR[51]. These findings are a potent marker of a better metabolic status with less anaerobic glycolysis.

Table 2 ROSC in diverse animal and human studies

First author	CPR method	ROSC (%)	↑ (%) with ITD	*P*-values
Animal studies				
Lurie *et al*[36]	ACD-CPR	77.8	28.5	0.18
	ACD-CPR + ITD	100		
Lurie *et al*[41]	S-CPR	18.2	199.5	< 0.05
	S-CPR+ITD	54.5		
Raedler *et al*[44]	S-CPR	0		
	ACD-CPR + ITD	42.9		0.06
Srinivasan *et al*[45]	S-CPR	37.5	166.7	< 0.05
	ACD-CPR + ITD	100		
Matsuura *et al*[52]	S-CPR	83.3	20.0	-
	S-CPR + ITD	100		
Human studies				
Vartanian *et al*[53]	S-CPR	45.0	31.1	0.03
	S-CPR + ITD	59.0		
Aufderheide *et al*[54]	S-CPR	33.8	12.1	0.022
	S-CPR + ITD	37.9		
Plaisance *et al*[55]	ACD-CPR	20.0	82.0	0.4
	ACD-CPR + ITD	36.4		
Wolcke *et al*[56]	S-CPR	37.0	48.6	0.016
	ACD-CPR + ITD	55.0		

ROSC: Return of spontaneous circulation.

Table 3 Patients discharged from hospitals with intact neurological function

First author	CPR method	Normal neurological function	*P*-values
Vartanian *et al*[53]	S-CPR	4/104	NS
	S-CPR + ITD	0/143	
Plaisance *et al*[55]	ACD-CPR	1/10	0.9
	ACD-CPR + ITD	1/11	
Wolcke *et al*[56]	S-CPR	4/75	0.4
	ACD-CPR + ITD	8/82	
Plaisance *et al*[62]	ACD-CPR	1/8	0.1
	ACD-CPR + ITD	6/10	

NS: Non significant.

Table 4 Hospital discharge rates in various human studies

First author	CPR method	Hospital discharge rates (%)	↑ (%) with ITD	*P*-values
Thigpen *et al*[58]	S-CPR	17.2	62	0.034
	S-CPR + ITD	27.9		
Davis *et al*[61]	S-CPR	20.7	73	< 0.001
	S-CPR + ITD	35.8		
Aufderheide *et al*[54]	S-CPR	7.9	98	< 0.001
	S-CPR + ITD	15.7		
Lurie *et al*[63]	S-CPR	9.3	83	0.0373
	S-CPR + ITD	17		

In addition, it has been demonstrated that after ROSC a rapid ice-cold saline infusion combined with ACD-CPR plus an ITD induces cerebral hypothermia more rapidly than standard CPR[45]. Table 2 shows the improvement of ROSC when ITD was implemented in CPR efforts.

CLINICAL STUDIES

The results of human clinical trials seem to reflect the data seen in animal models.

Standard CPR combined with an ITD

Systolic blood pressure was doubled when the ITD was used in 10 patients with out-of-hospital CA compared with similar patients treated with standard CPR[57]. Mean systolic blood pressure increased from 45 to 85 mmHg ($P < 0.001$) when a sham *vs* active ITD was used[57].

Adoption of the 2005 CPR guidelines and ITD resulted in a 75% increase in initial arrest survival rates and a 62% increase in survival to hospital discharge rates[58]. In a concurrent, randomized, blinded clinical trial focused on ICU admission rates, survival rates were higher in patients treated with standard CPR plus an ITD, especially in those who presented with pulseless electrical activity (over 100% increase in short-term survival)[59].

Moreover, adding an ITD to standard resuscitation care improved overall short-term survival by 50% and tripled survival in patients with traditionally the poorest outcomes, those with asystole[60]. No device-related adverse effects were observed.

Implementation of the 2005 AHA CPR guidelines together with an ITD resulted in a marked increase in in-hospital discharge rates of more than 70% when compared with historical controls in two large community hospitals[61].

The highest overall resuscitation rates in its 30-year history were observed when ITD was used by an EMS. The benefit was observed regardless of presenting rhythm. ROSC rates increased by 29% and neurologically intact discharge rates improved by > 50%[53]. Table 2 shows ROSC values in diverse studies when ITD was used in the respiratory circuit, while Table 3 shows hospital discharge of patients with intact neurological function.

Adoption of the ITD by 7 EMS systems who treated 893 CA victims with standard CPR, resulted in only a > 10% increase in ROSC rates but a doubling of hospital discharge rates, from 7.9% to 15.7% ($P < 0.001$)[54]. Table 4 shows hospital discharge rates in diverse studies.

ACD-CPR combined with an ITD

A study performed in prehospital mobile intensive care units in France was designed to evaluate acute hemodynamic parameters in non traumatic patients with prolonged CA treated with ACD-CPR alone or ACD-CPR plus an ITD[55]. The study demonstrated that use of an ITD during CPR further optimizes mechanical measures associated with ACD-CPR by increasing venous return and CPP. Diastolic arterial pressures and CPP were 70% higher than those achieved with ACD-CPR alone. In addition $PETCO_2$ levels were significantly higher when ITD was used[55].

The hemodynamic benefit observed in a previous

study was translated to a direct increase in survival rates and improved neurological function.

A prehospital clinical trial in Germany found significantly improved ROSC, 1 and 24-h survival rates when the combination of ACD-CPR and an ITD was compared with standard CPR alone (55% *vs* 37%, $P = 0.016$, 51% *vs* 32%, $P = 0.006$, 37% *vs* 22%, $P = 0.033$, respectively)[56]. One-hour and twenty four-hour survival rates in witnessed arrests were 55% and 41% with ACD CPR plus an ITD *vs* 33% and 23% in control subjects ($P = 0.011$ and 0.019), respectively. One-hour and twenty four-hour survival rates in patients with a witnessed arrest in ventricular fibrillation were 68% and 58% after ACD-CPR with an ITD *vs* 27% and 23% after standard CPR ($P = 0.002$ and 0.009, respectively). Survivors of this study treated with ACD-CPR plus an ITD had a marked improvement in their brain function at the time of hospital discharge[56].

Additional support for these findings was provided by another study which demonstrated that the combination of ACD-CPR and ITD in 400 patients with out-of hospital CA resulted in a doubling of 24-h survival[62]. In that study, patients were treated with either a sham or an active ITD. The neurologic function in the survivors was significantly better at hospital discharge in patients treated with the ITD.

A meta-analysis that included 833 patients from five high quality randomized studies concluded that the ITD consistently and significantly improved ROSC (46% for ITD group *vs* 36% for control, $P = 0.002$), early survival (32% *vs* 22%, $P = 0.0009$) and favorable neurologic outcome (13% *vs* 6%, $P = 0.004$)[64].

CONTROVERSIAL ITD STUDIES

An independent blinded study in a porcine model of CA tried to assess the effect of the ITD on CPP and passive ventilation (PaO_2 and $PaCO_2$) during standard CPR and its impact on the ROSC and short-term survival. In contrast to previous studies, use of the active ITD had no significant impact on CPP, passive ventilation, or outcomes compared to the sham device[65].

Furthermore, in a study by Menegazzi *et al*[66] use of the ITD during standard CPR did not improve CPP compared to standard CPR alone and also resulted in significantly lower ROSC and short term survival.

Finally, in a porcine model with a beating heart, use of an ITD combined with apnoeic oxygenation and without active ventilation during chest compressions resulted in hypoxemia due to transiently impaired lung function[67]. This study raised concerns from other investigators who claimed that Herff *et al*[67] misapplied the device and used a study design irrelevant to the recommended clinical use of the ITD, as an ITD is designed for patients in CA who are being actively ventilated[68].

CONCLUSION

Taken together, these observations suggest that enhancement of negative intrathoracic pressure during the decompression phase of CPR is associated with a marked cardiac preload. It is clear that priming the pump prior to cardiac defibrillation with the use of an ITD increases the chances for successful defibrillation. The hemodynamic benefits of the ITD during standard and ACD-CPR are striking in animals and in patients. Use of the ventilation timing lights on an ITD reduces the frequent, lethal rescuer error of hyperventilation. The ease of use of this device, its ability to be incorporated into a mask and other airway devices, the absence of device-related adverse effects and few requirements in additional training, suggest that ITD may be a favorable new device for improving CPR efficiency.

ITD offers new hope for survival in patients experiencing CA. Improved vital organ perfusion during CPR with the ITD is an important advance in resuscitation but it should be always kept in mind that by itself the ITD is not a panacea. It should be coupled with excellent preresuscitation and postresuscitation care to achieve better outcomes.

Since the literature is still short of studies with clinically meaningful outcomes such as neurological outcome and long term survival, further evidence is still needed.

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