American Red Cross Advisory Council on First Aid, Aquatics, Safety and Preparedness

ACFASP Scientific Review

Impedance Threshold Device

Questions to be addressed:

Impedance Threshold devices – should they be included in pre-hospital cardiac arrest management? This includes a literature review of prehospital basic responders, and advanced paramedic responders.

Introduction/Overview:

Based on promising data from animal models and studies, along with two randomized control studies included in this current review *[Wolcke, Circulation, 2003 & Plaisance, Resuscitation, 2004],* the 2005 American Heart Association/International Liaison Committee on Resuscitation (AHA/ILCOR) guidelines included the Impedance Threshold Valve Device [ITD] as a class IIa recommendation. Evidence showed that the ITD improved hemodynamic parameters, rates of Return of Spontaneous Circulation [ROSC] and 24 hour survival rates when compared to standard CPR alone. These studies did not show significantly improved rates of hospital discharge with favorable neurologic status, but may have been too small to show a significant difference. It was recognized that these long-term benefits [i.e. to hospital discharge, neurologic recovery] had not yet been completely addressed in the literature, and that future studies were needed.

This current ACFASP review looks at the literature involved in that 2005 statement and research published since then.

We are aware of a large multicentered study comparing standard CPR to standard CPR + ITD, which has recently been completed but not yet published. The preliminary results [https://roc.uwctc.org/tiki/tiki-index.php] last accessed on 20 April 2010, documents that recruitment was ceased because there was similar survival rates of patients with equally-preserved neurologic function between both groups. That research has not yet been published and subject to peer review.

Review Process and Literature Search Performed

Cochrane – no data on 'impedance threshold device' – closest review is on 'active compression/decompression CPR' which showed no clear benefit – data in this review is not directly transferable to the ITD although some of the physiological changes may be similar

Pubmed - ("electric impedance"[MeSH Terms] OR ("electric"[All Fields] AND "impedance"[All Fields]) OR "electric impedance"[All Fields] OR "impedance"[All Fields]) AND threshold[All Fields] AND ("equipment and supplies"[MeSH Terms] OR ("equipment"[All Fields] AND "supplies"[All Fields]) OR "equipment and supplies"[All Fields] OR "device"[All Fields]) AND ("cardiopulmonary resuscitation"[MeSH Terms] OR ("cardiopulmonary"[All Fields] AND "resuscitation"[All Fields]) OR "cardiopulmonary resuscitation"[All Fields] OR "cpr"[All Fields]).

Review of references in all articles, as well as bibliography at manufactures website www.advancedcirculatory.com – last accessed 20 April 2010, bibliography dated July 2008.

Abstracts were excluded.

Scientific Foundation:

The Impedance Threshold Device [ITD] is a valve that fits on the end of a Bag Valve Mask [BVM] and can attach to both standard endotracheal tubes and face masks. It has two main features:

1) the valve provides greater negative intrathoracic pressure during relaxation phase of chest compression if the circuit is kept sealed with a 'cracking' pressure of – 10 cm H2O, and
2) a timing light designed to remind rescuers of appropriate ventilation rates and avoid over-ventilation [10 breaths per minute]

There are multiple animal studies [swine] indicating that use of an ITD improves multiple physiological parameters during cardiac arrest *[Langhelle, Resus 2002, LOE 4; Lurie, Circ 1995, LOE 4; Lurie, Chest 1998, LOE 4; Lurie, Resp Care 2008, LOE 4; Yannopolous, Crit Care Med 2006, LOE 4; Yannopolous, Circ 2005, LOE 4; Yannopolous, Resus 2004, LOE 4].* Some of these swine studies also indicate improved survival at 24 hours *[Lurie, Circ 2002, LOE 4; Mengazzi, Prehosp Emerg Care, 2007; Srinivasen, J Am Coll Cardio 2006, LOE4].* There is some evidence from swine studies with improved neurological outcomes *[Lurie, Circ 2002, LOE 4].* There are some studies showing no benefit or harm with ITD *[Herff, Resus 2007, LOE 4; Madar, Resus 2008; LOE 4]*.

Many authors have provided reviews and expert opinion in support of ITD in cardiac arrest *[Frascone, Curr Op Crit Care 2004, LOE 5; Gabrielli, Curr Op Crit Care 2002, LOE 5; Lurie, Resus 2000, LOE 5, Lurie Crit Care Med, 2000, LOE 5; Lurie Minn Med 2002, LOE 6; Lurie Emerg Med Clinic North Am 2002, LOE 6; Pirrachio, Curr Op Crit Care, 2007; Ramsay, Am Surg, 2009m, LOE 5, Yannopolous, Euro Soc Cardio 2007, LOE 6]*

Other authors have commented on the need for long-term outcome studies *[Goodrich ACCN Adv Crit Care 2009, LOE 5].*

Published human studies have short-term end points, but generally also show enhanced physiological parameters *[Pirallo, Resus 2005, LOE 1b; Plaisance, Circ 2000, 1b], improved Return of Spontaneous Circulation [ROSC], and improved early survival [Aufderheide, Crit Care Med 2005, LOE 1a; Cabrini, Crit Care Med 2008, LOE 1a, Plaisance, Resus 2004, LOE 1a; Thayne, Resus 2005, LOE 1a; Wolke, Circ 2003, 1a].*

Although these studies did show effect on physiologic parameters, there was only a 'trend' to improved neurologic outcome and discharge from hospital.

Five key studies and one meta-analysis of those 5 studies:

Auferderheide, Crit Care Med, 2005 – Single EMS system, prospective, randomized, double-blind, intention-to-treat study comparing prehospital non-traumatic cardiac arrests treated with standard CPR vs. Standard CPR + ITD. 116 patients treated with sham device, 114 with active ITD. No difference in overall ICU admission, overall survival rates, but post-hoc analysis of presenting rhythm showed improved outcome for patients initially in PEA. There was no statistically significant difference for patients in ventricular fibrillation or asystole.

Cabrini, Crit Care Med 2008 – meta-analysis of 5 high quality randomized control studies *[Aufderheide, Crit Care Med, 2005; Pirrallo, Resus, 2005; Plaisance, Circ, 2000; Plaisance, Resus, 2004; Wolcke, Circ, 2003]* including 833 patients with 46% of patients with ITD achieving ROSC vs. 36% for control [p=0.002]. Improved early survival [32% with ITD vs 22% control, p=0.009]. Improved neurologic outcome for all early survivors [13% with ITD vs. 6% control, p=0.004]. However, no statistical effect on favorable neurologic outcome in survivors or improved survival at longest available follow up. See appendix for Forest Plot.

Pirralle Resus 2005 – Prospective, randomized, double-blind, intention-to-treat study in single EMS system involving endotracheal intubation of non-traumatic cardiac arrest comparing ITD device vs. identical ITD sham. Comparison of blood pressure after ROSC in the two groups, significantly improved SBP at 0, 2, 5 and 7 minutes after ROSC [roughly 30 mmHg greater in the ITD arm, p<0.01]. No report on survival.

Plaisance, Circ, 2000 – Prospective, randomized, blinded trial in prehospital mobile intensive care units in Paris, France. Nontraumatic cardiac arrests received ACD CPR +/- ITD. Comparison of ETCO2, DBP, CPP, time to ROSC showed significant improvements with ACD CPR + ICD. 2/10 patients in ACD CPR group had ROSC after 26.5 +/-0.7 minutes, which 4/11 patients in ACD CPR + ITD had ROSC 19.8 +/- 2.8 minutes. No survival outcomes described.

Plaisance, Resus, 2004 – single EMS system with 400 patients, compared their standard ACD-CPR to ACD-CPR with ITD, primary endpoint was survival to 24 hours. Statistically significant 24 hours survival with ITD [44/200 or 22% with sham and 64/200 or 32% with active device, p=0.02]. Also improvement in rate of ROSC [39% vs. 48%, p =0.05], ICU admission [29% vs. 40%, p=0.02] but no improvement in hospital discharge rates [4% vs. 5%, p=0.60].

Wolcke, Circ 2003 – prospective controlled trial in single EMS system for non-traumatic cardiac arrest randomized to ACD CPR + ITD or standard CPR after intubation. Statically improved rates of ROSC, 1- and 24-hour survival rates. However, hospital discharge rates were no different, 18% in ACD CPR + ITD and 13% in standard CPR population [p=0.41].

Other considerations:

While most studies used the ITD in conjunction with endotracheal intubation, there is some evidence that use with a closed circuit face mask and BVM also provides benefit physiologically *[Plaisance, Crit Care Med, 2005, 1b].* However, there is no evidence that addition of an ITD to standard BLS care [Face mask with BVM or mouth-to-mouth] provides additional benefit.

There is also preliminary evidence in a massive multi-centered study not yet subject to peer review that the ITD does not improve functional survival to hospital discharge.
We need to understand if using this device in routine prehospital non-traumatic cardiac arrest situations will provide better patient outcomes. While short-term markers may be helpful, long term outcomes are more important.

Overall Recommendation:

Use of an Impedance Threshold Device at -10cmH2O improves short term outcomes when used in non-traumatic cardiac arrests in conjunction with endotracheal intubation. There is no published evidence that long term survival [> 24 hours] is improved with the use of an ITD.
There is no evidence that the ITD in BLS care provides additional benefit.

Recommendations and Strength (using table below):

Standards: None

Guidelines: None

Options: In advanced life support with endotracheal intubation, the use of an ITD may be considered as part of a comprehensive system where other features of strong cardiac arrest management are ensured.

Summary of Key Articles/Literature Found and Level of Evidence/Bibliography:

	Author(s)	Full Citation	Summary of Article (provide a brief summary of what the article adds to this review)	Level of Evidence (Using table below)
1	AHA	AHA CPR techniques and Devices. Circulation 2005; 112; IV-47 – IV-50	2005 guidelines	5
2	Aufderheide TP, Kudenchuk PJ, Hedges JR, Nichol G, Kerber RE, Dorian P, Davis DP, Idris AH, Callaway CW, Emerson S, Stiell IG, Terndrup TE; ROC Investigators	Resuscitation Outcomes Consortium (ROC) PRIMED cardiac arrest trial methods part 1: rationale and methodology for the impedance threshold device (ITD) protocol. Resuscitation. 2008 Aug;78(2):179-85. Epub 2008 May 19. PubMed PMID: 18487005.	Publication outlining research protocol, outcome measures and expectations for a study. No data presented.	N/A
3	Aufderheide TP, Lurie KG.	Vital organ blood flow with the impedance threshold device. Crit Care Med. 2006 Dec;34(12 Suppl):S466-73. Review. PubMed PMID: 17114979.	Review article of current literature regarding ITD, includes association with active compression/decompression device. Not a meta analysis, but restates conclusions from other studies that CPR + ITD improves vital organ perfusion, and increased short-term survival rate.	5 – ITD improves vital organ perfusion
4	Aufderheide TP, Pirrallo RG, Provo TA, Lurie KG.	Clinical evaluation of an inspiratory impedance threshold device during standard cardiopulmonary resuscitation in patients with out-of-hospital cardiac arrest. Crit Care Med. 2005 Apr;33(4):734-40. PubMed PMID: 15818098.	A Key Study. Prospective, randomized, double-blind, intention-to-treat study in a pre-hospital EMS system using endotracheal intubation [not M-T-M or BVM]. Cardiac arrest of presumed cardiac etiology. Compared standard resuscitation with an active or sham impedance threshold device. Overall rates of ROSC and admission to ICU were the same for all population, but subgroup analysis showed that PEA patients had statistically greater chances of admission to an ICU and survival to 24 hours with the active device.	1a - survival to ICU and 24 hours for PEA patients in subgroup analysis
5	Böttiger BW, Groeben H, Schäfer M, Heine J.	["Highlights" in emergency medicine -- severe head trauma, polytrauma and cardiac arrest]. Anasthesiol Intensivmed Notfallmed Schmerzther. 2005 Jan;40(1):6-17. Review. German. PubMed PMID: 15645382.		

6	Cabrini L, Beccaria P, Landoni G, Biondi-Zoccai GG, Sheiban I, Cristofolini M, Fochi O, Maj G, Zangrillo A.	Impact of impedance threshold devices on cardiopulmonary resuscitation: a systematic review and meta-analysis of randomized controlled studies. Crit Care Med. 2008 May;36(5):1625-32. PubMed PMID: 18434910.	2007 systematic review and meta-analysis of ITD, included 5 studies and 833 patients – shows significantly improved rate of ROSC, early survival [not defined], and favorable neurologic outcome for all CPR patients. No difference for favorable neurologic outcome for survivors only, or survival at longest follow-up	1a – supportive for ROSC, early survival, but not for long term neurologic outcome in survivors
7	Convertino VA, Ratliff DA, Eisenhower KC, Warren C, Doerr DF, Idris AH, Lurie KG.	Inspiratory impedance effects on hemodynamic responses to orthostasis in normal subjects. Aviat Space Environ Med. 2006 May;77(5):486-93. PubMed PMID: 14708528	Not relevant – ITD impact on orthostatic hypotension for astronauts	n/a
8	Frascone RJ, Bitz D, Lurie K.	Combination of active compression decompression cardiopulmonary resuscitation and the inspiratory impedance threshold device: state of the art. Curr Opin Crit Care. 2004 Jun;10(3):193-201. Review. PubMed PMID: 15166836.	Review article [2004] of literature in support of active compression/decompression CPR with ITD. Evidence [sited in ACFASP review] that animal studies show improved blood flow to vital organs. Review of French literature in support of ACD-CPR with ITD with improved 1-hour and 24-hour survival rate, no statistical difference in discharge rates. ** unable to find Plaisance Circulation 2001 ref 40	5
9	Gabrielli A, Layon AJ, Wenzel V, Dorges V, Idris AH.	Alternative ventilation strategies in cardiopulmonary resuscitation. Curr Opin Crit Care. 2002 Jun;8(3):199-211. Review. PubMed PMID: 12386498.	Review article [2002] of airway management, LMA, combitube and introduction of ITD device – no new data presented	5
10	Goodrich C.	Cardiopulmonary resuscitation: where are we now? AACN Adv Crit Care. 2009 Oct- Dec; 20(4):373-83. PubMed PMID: 19893377.	Review article [2009] of active compression/decompression CPR, LifeBelt, AutoPulse and ITD – reviews Afderheide's 2005 work – 'inconclusive evidence'	5
11	Herff H, Raedler C, Zander R et al	Use of an inspiratory impedance threshold valve during chest compressions without assisted ventilations may result in hypozaemia. Resuscitation 2007; 72(3): 466-76	Swine model using alive swine with active beating hears and unusually high cracking pressures with an ITD. Compares physiological parameters when a live animal undergo various types of CPR with or without an ITD. Evidence that high 'cracking' pressures with an ITD impair pulmonary function. Further commentary regarding caution with high 'cracking' pressures.	4
12	Langhelle A, Strømme T, Sunde	Inspiratory impedance threshold valve during CPR. Resuscitation.	Porcine model with cross-over design measuring physiological parameters –	4

	K, Wik L, Nicolaysen G, Steen PA.	2002 Jan;52(1):39-48. PubMed PMID: 11801347.	improved myocardial blood flow when added to standard CPR	
13	Lurie K, Voelckel W, Plaisance P, Zielinski T, McKnite S, Kor D, Sugiyama A, Sukhum P.	Use of an inspiratory impedance threshold valve during cardiopulmonary resuscitation: a progress report. Resuscitation. 2000 May;44(3):219-30. Review. PubMed PMID: 10825624.	Review article [2000] of animal and human studies on ITD to date – no new data presented – recognizes need for research on long-term benefits	4
14	Lurie K, Zielinski T, McKnite S, Sukhum P.	Improving the efficiency of cardiopulmonary resuscitation with an inspiratory impedance threshold valve. Crit Care Med. 2000 Nov;28(11 Suppl):N207-9. PubMed PMID: 11098948.	Review article [2000] of animal and French Clinical data – recognizes physiological effects, and need for further work on human outcomes	5
15	Lurie K.	Bringing back the nearly dead. The hope and the challenge. Minn Med. 2002 Apr;85(4):39-42. PubMed PMID: 1975053.	Commentary of continued efforts to improve cardiac arrest outcomes. No new data presented.	6
16	Lurie K.	Mechanical devices for cardiopulmonary resuscitation: an update. Emerg Med Clin North Am. 2002 Nov;20(4):771-84. Review. PubMed PMID: 12476879.	Review article similar to others by this author. No new data.	4
17	Lurie KG, Coffeen P, Shultz J, McKnite S, Detloff B, Mulligan K.	Improving active compression-decompression cardiopulmonary resuscitation with an inspiratory impedance valve. Circulation. 1995 Mar 15;91(6):1629-32. PubMed PMID: 7882467	Porcine model measuring cerebral and coronary perfusion, as well as defib success rates, in ACD-CPR +/- ITD – addition of ITD improves vital organ perfusion and defibrillation	4
18	Lurie KG, Mulligan KA, McKnite S, Detloff B, Lindstrom P, Lindner KH.	Optimizing standard cardiopulmonary resuscitation with an inspiratory impedance threshold valve. Chest. 1998 Apr;113(4):1084-90. PubMed PMID: 9554651.	Porcine model comparing physiological effects during cardiac arrest of CPR alone vs. CPR+ITD – improved vital organ flow	4
19	Lurie KG, Yannopoulos D, McKnite SH, Herman ML, Idris AH, Nadkarni VM, Tang W, Gabrielli A, Barnes TA, Metzger AK.	Comparison of a 10-breaths-per-minute versus a 2-breaths-per-minute strategy during cardiopulmonary resuscitation in a porcine model of cardiac arrest. Respir Care. 2008 Jul;53(7):862-70. PubMed PMID: 18593487.	Porcine model comparing various rates of ventilation with CPR +/- ITD device – addition of ITD device improved organ perfusion	4
20	Lurie KG, Zielinski	Use of an inspiratory impedance	Porcine model with 24 hour survival and	4

	T, McKnite S, Aufderheide T, Voelckel W	valve improves neurologically intact survival in a porcine model of ventricular fibrillation. Circulation 2002; 105:124-129	neurologic indices for ventricular fibrillation and resuscitation with CPR +/- ITD – greater survival from initial arrest and greater 24-hour neurological scores in ITD pigs	
21	Lurie KG, Zielinski TM, McKnite SH, Idris AH, Yannopoulos D, Raedler CM, Sigurdsson G, Benditt DG, Voelckel WG.	Treatment of hypotension in pigs with an inspiratory impedance threshold device: a feasibility study. Crit Care Med. 2004 Jul;32(7):1555-62. PubMed PMID: 15241102.	Porcine model investigating physiological parameters in pigs subjected to hemorrhage [not cardiac arrest] – no new data on CPR or cardiac arrest presented	4
22	Mader TJ, Kellogg AR, Smith J, Hynds-Decoteau R, Gaudet C, Caron J, Murphy B, Paquette A, Sherman LD.	A blinded, randomized controlled evaluation of an impedance threshold device during cardiopulmonary resuscitation in swine. Resuscitation. 2008 Jun;77(3):387-94. Epub 2008 Mar 4. PubMed PMID: 18308451.	Swine model with 30 swing. Induced ventricular fibrillation, untreated for 8 minutes, then S-CPR, either with ITD or without. Baseline characteristics similar, there was no difference in measured outcomes [CPP, PaCO2, PaO2 or ROSC].	4
23	Menegazzi JJ, Salcido DD, Menegazzi MT, Rittenberger JC, Suffoletto BP, Logue ES, Mader TJ.	Effects of an impedance threshold device on hemodynamics and restoration of spontaneous circulation in prolonged porcine ventricular fibrillation. Prehosp Emerg Care. 2007 Apr-Jun;11(2):179-85. PubMed PMID: 17454804.	Porcine model with 36 animals, case controlled design nested within a randomized primary study. Standard CPR +/- ITD. ITD-CPR did no improve CPP compared to S-CPR. ROSC and survival were significantly lower with ITD-CPR.	4
24	Pilvinis V, Vaitkaitis D, Stasiukyniene V, Pranskūnas A.	[Physiological aspects of cardiopulmonary resuscitation in adults]. Medicina (Kaunas). 2006;42(4):346-53. Review. Lithuanian. PubMed PMID: 16687907.		
25	Pirracchio R, Payen D, Plaisance P.	The impedance threshold valve for adult cardiopulmonary resuscitation: a review of the literature. Curr Opin Crit Care. 2007 Jun;13(3):280-6. Review. PubMed PMID: 17468559.	Review Article [2007] supporting role of ITD in enhancing preload by decreasing intrathoracic pressure improves overall cardiopulmonary efficacy. No new data presented.	5
26	Pirrallo RG, Aufderheide TP, Provo TA, Lurie KG.	Effect of an inspiratory impedance threshold device on hemodynamics during conventional manual cardiopulmonary resuscitation. Resuscitation. 2005 Jul;66(1):13-	Prospective randomized, double-blind, intention-to-treat study in a single EMS system. EMS personnel performed endotracheal intubation and regular CPR vs. CPR with ITD. Invasive femoral artery BP measurement found improved femoral BP in	1b

		20. PubMed PMID: 15993724.	ITD patients vs. regular CPR.	
27	Plaisance P, Lurie KG, Vicaut E, Martin D, Gueugniaud PY, Petit JL, Payen D.	Evaluation of an impedance threshold device in patients receiving active compression-decompression cardiopulmonary resuscitation for out of hospital cardiac arrest. Resuscitation. 2004 Jun;61(3):265-71. PubMed PMID: 15172704.	A key article. Multicentered clinical randomized controlled blinded prospective trial comparing 'standard care' [endotracheal intubation and active compression-decompression (ACD) CPR] with or without an ITD device. Physician led ALS team, roughly 18 minute EMS response time. 200+200 patients. Primary endpoint = survival at 24 hours. 32% survival for the active ITD device group vs 22% survival in the sham group [p = 0.02]. There was no difference in rates of hospital discharge [5% ITD vs. 4% sham, P=0.63]. 6/10 survivors in active group had normal neurologic function, vs. 1/8 in the sham group [p = 0.1].	1a
28	Plaisance P, Lurie KG, Payen, D.	Inspiratory Impedance During Active Compression decompression Cardiopulmonary Resuscitation: A randomized Evaluaion in Patients in Cardiac Arrest. Circulation. 2000; 101:989-994	Prospective, randomized, blinded trial for 33 patients in non-traumatic cardiac arrest, comparison of ACD-CPR with or without ITD. Physiologic parameters measured showed statistically significant [p<0.001] for maximal ETCO2, CPP, and diastolic arterial pressures. ACD-CPR + ITD group has faster intubation to ROSC times [26.5 +/- 0.7 min vs. 19.8 +/- 2.8 min, p<0.05].	1b
29	Plaisance P, Soleil C, Lurie KG, Vicaut E, Ducros L, Payen D.	Use of an inspiratory impedance threshold device on a facemask and endotracheal tube to reduce intrathoracic pressures during the decompression phase of active compression-decompression cardiopulmonary resuscitation. Crit Care Med. 2005 May;33(5):990-4. PubMed PMID: 15891326.	Small [16 patient] blinded randomized control study looking at airway pressures during cardiac arrest treatment with ACD-CPR, and the addition of an ICD to endotracheal tubes or regular BVM with face mask. Airway pressures were shown to be similar with ITD, regardless of endotracheal intubation or face mask. No measurements of outcome.	1b
30	Ramsay PT, Maxwell RA.	Advancements in cardiopulmonary resuscitation: increasing circulation and improving survival. Am Surg. 2009 May; 75(5): 359-62 PUBMED PMID: 19445283	Review article 'invited commentary' enforcing that any resuscitation is better than nothing, and reviewing again ITD papers showing improved physiological parameters.	5
31	Sigurdsson G, Yannopoulos D, McKnite SH, Sondeen JL, Benditt DG, Lurie KG.	Effects of an inspiratory impedance threshold device on blood pressure and short term survival in spontaneously breathing hypovolemic pigs.	Swine model investigating role of ITD in hemorrhagic shock where pigs were bled 50% of blood volume, endotracheal intubation, followed by ventilation with or without ITD. Lower airway pressure, improved arterial	4

		Resuscitation. 2006 Mar;68(3):399-404. Epub 2006 Feb 7. PubMed PMID: 16455176.	pressures. All pigs in control group died, 7/8 in ITD groups survived >90 min, 6/8 woke up with 'no neurologic deficit'.	
32	Srinivasan V, Nadkarni VM, Yannopoulos D, Marino BS, Sigurdsson G, McKnite SH, Zook M, Benditt DG, Lurie KG.	Rapid induction of cerebral hypothermia is enhanced with active compression-decompression plus inspiratory impedance threshold device cardiopulmonary resusitation in a porcine model of cardiac arrest. J Am Coll Cardiol. 2006 Feb 21;47(4):835-41. Epub 2006 Jan 26. PubMed PMID: 16487853.	Swine model where cerebral temperatures were measured during VF with endotracheal intubation, and ice-cold saline flush. Compared groups of standard CPR vs. ACD-CPR + ITD. Statistically better 1) Right atrial pressure [p<0.01] 2) Coronary perfusion pressure for ACD-ITD CPR [p<0.01] and 3) rate of cerebral cooling [p<0.005]. All 8/8 ACD-ITD CPR pigs survived with ROSC within 15 minutes, with 3/8 in standard treatment survived [p<0.05].	4
33	Thayne RC, Thomas DC, Neville JD, Van Dellen A.	Use of an impedance threshold device improves short-term outcomes following out-of-hospital cardiac arrest. Resuscitation. 2005 Oct;67(1):103-8. PubMed PMID: 16150530.	A key article. Implementation of the ITD protocol in an EMS system with before and after analysis of rate of admission to the ED. Intervention included retraining of paramedics to 1) use the ITD after endotracheal intubation 2) allow chest to fully recoil with CPR 3) follow timing light of ITD to avoid over-ventilation 4) other features of improved CPR Comparison with matched controls from previous year. Improved rate of admission to ER alive with improved CPR + ITD [34% survival to hospital with intervention compared to 22% in historical control, p<0.01]. Asystole patients also had improved survival [34% with intervention vs. 11% without, p<0.01]	1a
34	Voelckel WG, Yannopoulos D, Zielinski T, McKnite S, Lurie KG.	Inspiratory impedance threshold device effects on hypotension in heat-stroked swine. Aviat Space Environ Med. 2008 Aug;79(8):743-8. PubMed PMID: 18717111.	Swine model of induced heat-stroke associated hypotension followed by arterial pressure changes related to application of an ITD. No direct relation to question.	n/a
35	Wigginton JG, Miller AH, Benitez FL, Pepe PE.	Mechanical devices for cardiopulmonary resuscitation. Curr Opin Crit Care. 2005 Jun;11(3):219-23. PubMed PMID: 15928469.	Review of current literature around devices for CPR – no new data presented.	n/a
36	Wolcke BB, Mauer DK, Schoefmann MF, Teichmann H, Provo TA, Lindner KH, Dick WF, Aeppli D, Lurie KG.	Comparison of standard cardiopulmonary resuscitation versus the combination of active compression-decompression cardiopulmonary resuscitation and an inspiratory impedance threshold device for out-of-	A key article. Prospective, controlled trial comparing standard CPR to ACD + ITD CPR. CPR type changed with each shift. Primary end point = survival to one hour. Secondary end points = ROSC, survival to 24 hours, survival to hospital discharge, neurological recovery. Improved one hour survival [55% vs 33%	1a

		hospital cardiac arrest. Circulation. 2003 Nov 4;108(18):2201-5. Epub 2003 Oct 20. PubMed PMID: 14568898.	p=0.011] and 24 hour survival [41% vs. 23%, p=0.019]. Greater benefit for VF patients. No significant difference in hospital discharge rates [18% vs 13%, p=0.41]. Improved neurologic function in witnessed arrests [p-0.07]	
37	Yannopoulos D, Aufderheide T.	Acute management of sudden cardiac death in adults based upon the new CPR guidelines. Europace. 2007 Jan;9(1):2-9. Review. PubMed PMID: 17224415.	Review article outlining key changes in CPR with 2005 AHA guidelines, focused on early defibrillation, uninterrupted Compressions, complete decompression, fewer ventilations. No new data presented.	6
38	Yannopoulos D, Aufderheide TP, Gabrielli A, Beiser DG, McKnite SH, Pirrallo RG, Wigginton J, Becker L, Vanden Hoek T, Tang W, Nadkarni VM, Klein JP, Idris AH, Lurie KG.	Clinical and hemodynamic comparison of 15:2 and 30:2 compression-to-ventilation ratios for cardiopulmonary resuscitation. Crit Care Med. 2006 May;34(5):1444-9. PubMed PMID: 16557155.	Prospective randomized swine model to review impact of ITD on intracranial pressure [ICP] in normovolemic and hypovolemic pigs. Postulated that increased ICP is associated with worse outcomes, and lowering ICP may improve neurological outcome. Data presented shows that ICP decreases with ITD in multiple situations, and hypothesized that lower ICP results in improved CPP.	4
39	Yannopoulos D, Aufderheide TP.	Use of the Impedance Threshold Device (ITD). Resuscitation. 2007 Oct;75(1):192-3; author reply 193-4. Epub 2007 Jun 18. PubMed PMID: 17574321.	Letter commenting on ITD study by Herff [above]	n/a
40	Yannopoulos D, McKnite SH, Metzger A, Lurie KG.	Intrathoracic pressure regulation for intracranial pressure management in normovolemic and hypovolemic pigs. Crit Care Med. 2006 Dec;34(12 Suppl):S495-500. PubMed PMID: 17114984.	Prospective swine model with different compression to ventilation ratios [15:2 vs 30:2] with and without an ITD. Measurement of acid-base status, cerebral and cardiovascular parameters. Documents improved parameters with 30:2 compression ratio in swine, and improved parameters with addition of ITD.	4
41	Yannopoulos D, Nadkarni VM, McKnite SH, Rao A, Kruger K, Metzger A, Benditt DG, Lurie KG.	Intrathoracic pressure regulator during continuous-chest-compression advanced cardiac resuscitation improves vital organ perfusion pressures in a porcine model of cardiac arrest. Circulation. 2005 Aug 9;112(6):803-11. Epub 2005 Aug 1. PubMed PMID: 16061732.	Swine model with induced VF, endotracheal intubation. Compared standard CPR with ITD-CPR. Improved physiological parameters, and improved 1 hour survival with ITD-CPR [P=0.01].	4
42	Yannopoulos D, Sigurdsson G, McKnite S, Benditt	Reducing ventilation frequency combined with an inspiratory impedance device improves CPR	Swine model reviewing physiological parameters with different rates of compression and ventilation with and without	4

	D, Lurie K	efficiency in swine model of cardiac arrest. Resuscitation 61 (2004) 75-82	an ITD. Improved CPP, MAP and ETCO2 when 10:1 c:v ratio and ITD [p=0.01].	
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Level of Evidence	Definitions **(See manuscript for full details)**
Level 1a	**Experimental and Population based studies -** population based, randomized prospective studies or meta-analyses of multiple higher evidence studies with substantial effects
Level 1b	**Smaller Experimental and Epidemiological studies -** Large non-population based epidemiological studies or randomized prospective studies with smaller or less significant effects
Level 2a	**Prospective Observational Analytical** - Controlled, non-randomized, cohort studies
Level 2b	**Retrospective/Historical Observational Analytical** - non-randomized, cohort or case-control studies
Level 3a	**Large Descriptive studies** – Cross-section, Ecological, Case series, Case reports
Level 3b	**Small Descriptive studies** – Cross-section, Ecological, Case series, Case reports
Level 4	**Animal studies or mechanical model studies**
Level 5	**Peer-reviewed Articles** - state of the art articles, review articles, organizational statements or guidelines, editorials, or consensus statements
Level 6	**Non-peer reviewed published opinions -** such as textbook statements, official organizational publications, guidelines and policy statements which are not peer reviewed and consensus statements
Level 7	**Rational conjecture** (common sense); common practices accepted before evidence-based guidelines
Level 1-6E	**Extrapolations** from existing data collected for other purposes, theoretical analyses which is on-point with question being asked. Modifier E applied because extrapolated but ranked based on type of study.

APPENDIX - Data extract from Meta-analysis

Impact of impedance threshold devices on cardiopulmonary resuscitation: A systematic review and meta-analysis of randomized controlled studies

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Objectives: Vital organ hypoperfusion significantly contributes to the dismal survival rates observed with manual cardiopulmonary resuscitation after cardiac arrest. The impedance threshold device is a valve which reduces air entry into lungs during chest recoil between chest compressions, producing a potentially beneficial decrease in intrathoracic pressure and thus increasing venous return to the heart. This review provides an update on the impedance threshold device and underlines its effect on short-term survival.

Data Source: MedCentral, CENTRAL, PubMed, and conference proceedings were searched (updated March 27, 2007). Authors and external experts were contacted.

Study Selections: Three unblinded reviewers selected randomized trials using an impedance threshold device in cardiopulmonary resuscitation of nontraumatic out-of-hospital cardiac arrests. Four reviewers independently abstracted patient, treatment and outcome data.

Data Extraction: A total of 833 patients from five high quality randomized studies were included in the analysis.

Data Synthesis: Pooled estimates showed that the impedance threshold device consistently and significantly improved return to spontaneous circulation (202/438 [46%] for impedance threshold device group vs. 159/445 [36%] for control, relative risk [RR] = 1.29 [1.10–1.51], $p = .002$), early survival (139/428 [32%] vs. 97/433 [22%], RR = 1.45 [1.16–1.80], $p = .0009$) and favorable neurologic outcome (39/307 [13%] vs. 18/293 [6%], RR = 2.36 [1.30–4.24], $p = .004$) with no effect on favorable neurologic outcome in survivors (39/60 [65%] vs. 18/44 [41%]) nor an improved survival at the longest available follow up (35/428 [8.2%] vs. 24/433 [5.5%]).

Conclusions: This meta-analysis of randomized controlled studies suggests that the impedance threshold device improves early outcome in patients with out-of-hospital cardiac arrest undergoing cardiopulmonary resuscitation. (Crit Care Med 2008; 36:1625–1632)

Key Words: impedance threshold devices; cardiopulmonary resuscitation; meta-analysis; systematic review; cardiac arrest; randomized trials

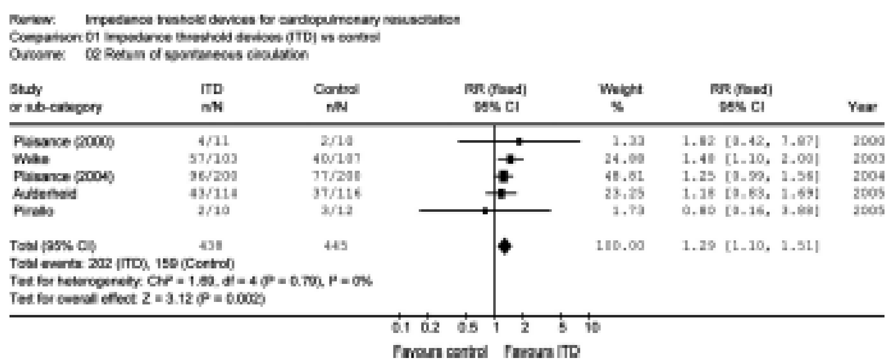

Figure 2. Forest plot for the comparison of impedance threshold devices vs. control on return of spontaneous circulation after cardiopulmonary resuscitation in five studies. *RR*, relative risk; *CI*, confidence interval.

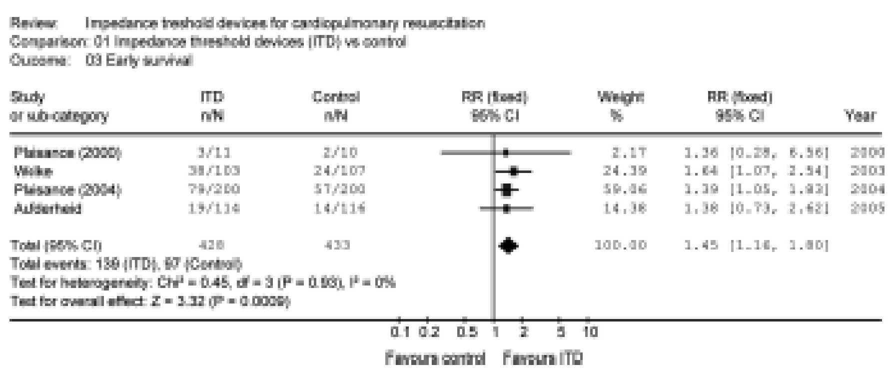

Figure 3. Forest plot for the comparison of impedance threshold devices vs. control on early survival after cardiopulmonary resuscitation in four studies. *RR*, relative risk; *CI*, confidence interval.