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

Luca Cabrini, MD; Paolo Beccaria, MD; Giovanni Landoni, MD; Giuseppe G. L. Biondi-Zoccai, MD; Imad Sheiban, MD; Marta Cristofolini, MD; Oliviero Fochi, MD; Giulia Maj, MD; Alberto Zangrillo, MD

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 = 2.35 [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

Cardiac arrest is a clinical condition still characterized by a poor prognosis (1, 2). In the last decades a huge attempt was performed in order to improve survival rate and outcome. An educational effort was conducted toward both healthcare providers and laymen. Cultural and technological progress enabled new therapeutic options as early defibrillation and therapeutic hypothermia; there was an improvement in the organizational area and new protocols for out-of-hospital and in-hospital environment were performed. Conversely, the pharmacologic approach did not change in its major settings (3).

Presently the most effective topics seem to be related to the rapidity of intervention, training, the use of in-hospital and out-of-hospital protocols, and improvement of coronary perfusion pressure.

Different devices to improve coronary perfusion pressure were proposed, but none of them has consistently been shown to be superior to conventional manual cardiopulmonary resuscitation (CPR), as presented in the last American Heart Association Guidelines for Resuscitation (3). Not even active compression-decompression (ACD), probably the most studied device, produced the expected benefits: a recent review from Cochrane did not show any evidence for its indication (4).

The impedance threshold device (ITD) is a valve which reduces air entry into lungs during chest recoil between chest compressions, producing a decrease in intrathoracic pressure and increasing venous return to the heart (5, 6). The effect is supposedly improved when its use is combined with ACD, enhancing venous return during active decompression (7).

The purpose of this meta-analysis is to update randomized controlled studies regarding ITD.

MATERIALS AND METHODS

Search Strategy. Pertinent studies were independently searched in BioMedCentral,

From the Department of Anesthesia and Intensive Care (LC, PB), Università Vita-Salute San Raffaele, Milano, Italia e Istituto Scientifico San Raffaele, Milan, Italy; the Department of Cardiothoracic Anesthesia and Intensive Care (GL, OF, GM, AZ), Università Vita-Salute San Raffaele, Milano, Italia e Istituto Scientifico San Raffaele, Milan, Italy; the Interventional Cardiology, Division of Cardiology (GGLB-Z, IS), Università di Torino, Torino, Italy; and the Department of Anestesia and Intensive Care (MC), Ospedale Santa Chiara, Trento, Italy.

The study was supported by departmental funds only.

The authors have not disclosed any potential conflicts of interest.

For information regarding this article, E-mail: landoni.giovanni@hsr.it

DOI: 10.1097/CCM.0b013e318170ba80

Table 1. Design features and appraisal of the internal validity of included studies[a]

Main Investigator	Publication Type	Multicenter Enrollment	Means for Allocation Concealment	Treatment Allocation	Risk of Selection Bias	Risk of Performance Bias	Risk of Attrition Bias	Risk of Detection Bias
Plaisance (2000)	Full paper	Yes	Sham device	Computer-generated randomization	A	A	A	A
Wolcke	Full paper	No	Randomization code broke after initial resuscitation	Computer-generated randomization (clustered by work shift)	B	B	A	B
Plaisance (2004)	Full paper	Yes	Sham device	Randomization	A	A	A	A
Aufderheide	Full paper	Yes	Sham device	Computer-generated randomization	A	A	A	A
Pirallo	Full paper	Yes	Sham device	Computer-generated randomization	A	A	A	A

[a]Risk of bias is expressed as A (low risk), B (moderate risk), C (high risk), and D (incomplete reporting leading to inability to ascertain the underlying risk of bias).

Table 2. Overall characteristics of 883 patients who received either ITD (438 patients) or control (in four of five cases a sham) for out-of-hospital cardiopulmonary resuscitation

First Author	N Patients	Age	Female	Witnessed Arrest	VF	PEA	Asystole	Call to BLS Arrival	Call to Device Arrival	Time to ALS Arrival
Plaisance (2000)	21	58	29%	71%	0%	0%	100%	6.6 min	NR	19.8 min
Wolcke	210	67	38%	75%	40%	30%	30%	6 min	9.5 min	NR
Plaisance (2004)	400	59	33%	75%	25%	4%	72%	8.6 min	NR	18 min
Pirrallo	22	61	41%	45%	18%	32%	45%	NR	19 min	8.7 min
Aufderheide	230	66	39%	59%	26%	23%	51%	4.7 min	12.2 min	6.8 min

N, number; VF, ventricular fibrillation; PEA, pulseless electrical activity; BLS, basic life support; ITD, impedance threshold device; ALS, advanced life support; Min, minutes; NR, not reported.

Table 3. Settings, number of patients (randomized to ITD or control treatment) and duration of cardiopulmonary resuscitation of patients with out of hospital cardiac arrest

First Author	Journal	Year	Full Paper or Abstract?	Setting	N ITD	N Controls	CPR Duration ITD Group (min)	CPR Duration Control Group (min)
Plaisance (2000)	*Circulation*	2000	Full paper	Out of hospital	11	10	26	29
Wolcke	*Circulation*	2003	Full paper	Out of hospital	103	107	35 ± 12	34 ± 13
Plaisance (2004)	*Resuscitation*	2004	Full paper	Out of hospital	200	200	29 ± 1	27 ± 1
Aufderheide	*Crit Care Med*	2005	Full paper	Out of hospital	114	116	31 ± 12	32 ± 11
Pirrallo	*Resuscitation*	2005	Full paper	Out of hospital	10	12	46 ± 10	44 ± 9.810

ITD, impedance threshold device; CPR, cardiopulmonary resuscitation.

CENTRAL, and PubMed (updated March 27, 2007) by several trained investigators (LC, GL, PB, OF). The full search strategies are available in the Appendix. Further hand or computerized searches involved the recent (2003–2006) conference proceedings from the International Anesthesia Research Society, American Heart Association, American College of Cardiology, American Society of Anesthesiology, and European Society of Cardiology congresses. In addition, we employed backward snowballing (i.e., scanning of references of retrieved articles and pertinent reviews) and contacted international experts for further studies. No language restriction was enforced, and non English-language articles were translated when appropriate.

Study Selection. References obtained from database and literature searches were first independently examined at the title/abstract level by several investigators (LC, GL, PB, OF) with divergences resolved by consensus, and then, if potentially pertinent, retrieved as complete articles.

The following inclusion criteria were employed for potentially relevant studies: a) random allocation to treatment, b) comparison of ITD vs. control treatment.

The exclusion criteria were: a) nonparallel design (i.e., crossover) randomized trials, b) duplicate publications (in this case only the article reporting the longest follow-up was abstracted), c) nonhuman experimental studies, d) no outcome data.

Two investigators (LC, GL) independently assessed compliance to selection criteria and selected studies for the final analysis, with divergences finally resolved by consensus (Table 1).

Data Abstraction and Study Characteristics. Baseline and outcome data were independently abstracted by several investigators (LC, GL, PB, OF) with divergences resolved by consensus (Table 2, Table 3, and Table 4). Specifically, we extracted study design (including patient selection and randomization), population, clinical setting, patients' characteristics (age, sex, rate of witnessed cardiac arrest, initial rhythm, call of basic life support, ITD, and advanced life support arrival), number of randomized patients, length of CPR, and major

Table 4. Details of treatment and control groups and of major complications

First Author	Treatment Group	Control Group	Rib Fractures ITD vs. Control	Pulmonary Edema ITD vs. Control	Vomiting ITD vs. Control	Witnessed Cardiac Arrest ITD vs. Control	Bystander CPR ITD vs. Control
Plaisance 2000	ACD-CPR + ITD	ACD-CPR + sham ITD	NR	NR	NR	71% vs. 60%	19% vs. 20%
Wolcke	ACD-CPR + ITD	Standard CPR	18 vs. 14	3 vs. 0	12 vs. 8	80% vs. 70%	29% vs. 27%
Plaisance 2004	ACD-CPR + ITD	ACD-CPR + sham ITD	78 vs. 60	8 vs. 14	NR	74% vs. 75%	10% vs. 10%
Aufderheide	Standard CPR + ITD	Standard CPR sham ITD	NR	9 vs. 6	14 vs. 9	59% vs. 59%	23% vs. 31%
Pirrallo	Standard CPR + ITD	Standard CPR sham ITD	0 vs. 0	2 vs. 5	1 vs. 2	45% vs. 50%	20% vs. 33%

ACD, active compression-decompression; ITD, impedance threshold device; CPR, cardiopulmonary resuscitation; NR, not reported.

complications (rib fractures, pulmonary edema, vomiting). At least two separate attempts at contacting original authors were made in case of missing data.

The primary end-points of the present review were early survival (at 24 hrs in three studies and at intensive care unit admission in one study) and return of spontaneous circulation (ROSC). Other relevant secondary endpoints were survival at the longest follow-up available for each study (1 yr [12], 30 days [13], and hospital discharge [7, 15]) and neurologic outcome. (Cerebral Performance Category neurologic scoring system: 1 = normal; 2 = mild cognitive impairment; 3 = major cognitive impairment; 4 = severe neurologic impairment; 5 = comatose.)

Internal Validity Assessment. The internal validity of included trials was appraised according to the Cochrane Collaboration methods, i.e., judging the risk for selection bias (i.e., the bias due to the unbalanced enrollment of specific patient subsets in one of the groups), performance bias (i.e., the bias due to differences in the management of patients or ancillary treatment, beyond the intervention object of randomized allocation), attrition bias (i.e., the bias due to incomplete follow-up or different length of follow-up), and adjudication bias (i.e., the bias due to unclear, implicit, or not universally employed definitions for adverse events), and expressed as low risk of bias (a), moderate risk of bias (b), high risk of bias (c), or incomplete reporting leading to inability to ascertain the underlying risk of bias (d) (34). In addition, allocation concealment explicitly distinguished as adequate (a), unclear (b), inadequate (c), or not used (d) (Table 1). Two independent and experienced reviewers (GL, GGLB-Z) appraised study quality, with divergences resolved by consensus.

Data Analysis and Synthesis. Binary outcomes from individual studies were analyzed in order to compute individual relative risks (RR) with pertinent 95% confidence intervals (CIs), and a pooled summary effect estimate was calculated by means of a fixed effects model, except in case of at least moderate (50%) statistical inconsistency (I2) when a random effect model was used (8). We assessed the robustness of findings from the primary analysis to the effects of study population and baseline risk for any of the primary outcomes through a series of sensitivity analyses, including random effects model, and by withdrawing one study at a time.

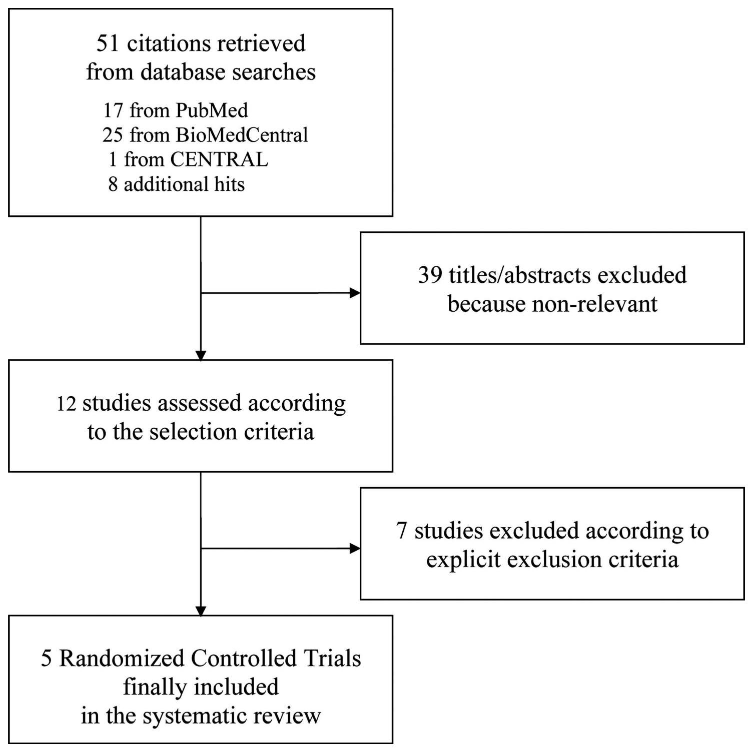

Figure 1. Flow chart of the systematic review process.

Statistical heterogeneity and inconsistency was measured using, respectively, Cochrane Q tests and I^2 (9). According to Higgings et al., I^2 values around 25%, 50%, and 75% were considered representing, respectively, low, moderate, and severe statistical inconsistency. The risk of small study bias (including publication bias) was assessed by visual inspection of funnel plots and computing the Egger test (10). Statistical significance was set at the two-tailed 0.05 level for hypothesis testing and at 0.10 for heterogeneity testing. Unadjusted p values are reported throughout. Computations were performed with SPSS 11.0 (SPSS, Chicago, IL, USA) and RevMan 4.2 (a freeware available from the Cochrane Collaboration) (11).

This study was performed in compliance with the Cochrane Collaboration and the Quality of Reporting of Meta-Analyses (QUOROM) guidelines.

Statement of Responsibility. The authors had full access to data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

RESULTS

Database searches, snowballing and contacts with experts yielded a total of 51 citations (Fig. 1). Excluding 46 nonpertinent titles or abstracts, we retrieved in complete form and assessed according to the selection criteria five studies (7, 12, 13, 14, 15), which were included in the final analysis after the correspondent authors confirmed that there was no overlapping and/or duplicate publication. Four of these five studies were identified through database searches, while snowballing identified the fifth study. Contact with experts and conference proceedings did not identify any further study.

Study Characteristics. The five randomized controlled studies included 883 patients (438 to ITD and 445 to the control group, in four of five cases a sham) (Table 4). All studies were performed in nontraumatic out-of-hospital adult patients and stated that the updated international basic life support and advanced life support guidelines were strictly followed. Patients characteristics, initial rhythm and time to basic life support, ITD, and advanced life support are illustrated in Table 2. CRP duration, main complications, and percentage of witnessed cardiac arrest of bystander CPR did not differ in the two groups and are illustrated in Tables 3 and 4.

All studies were of high quality (Table 1) as testified by the details on the method used for randomized sequence generation and allocation, adequate allocation concealment, and low risk of selection, performance, attrition and detection bias. All but one study employed a multicenter design, a feature which does not strictly impact on internal validity, but usually increases external validity of a trial. All studies reported on ROSC, while only four out of five studies reported data on mortality and neurologic outcomes. (7, 12, 13, 15).

Quantitative Data Synthesis. Overall analysis showed that, in comparison to control treatment, ITD was associated with clinically relevant benefits on all major end points. Specifically, ITD increased ROSC (202/438 [46%] in the ITD group vs. 159/445 [36%] in the control arm, RR = 1.29 [1.10–1.51], p for effect = 0.002, p for heterogeneity = 0.79, I^2 = 0%) (Fig. 2), and early survival (139/428 [32%] vs. 97/433 [22%], RR = 1.45 [1.16–1.80], p for effect = 0.0009, p for heterogeneity = 0.93, I^2 = 0%) (Fig. 3).

There was no significant difference with regards to a more favorable neurologic outcome (Cerebral Performance Category neurologic scoring system 1 [12, 13] or 1 plus 2 [7, 15]) in survivors (39/60 [65%] vs. 18/44 [41%], RR = 1.65 [0.65–4.16], p for effect = .29, p for heterogeneity = .02, I^2 = 70% [Fig. 4] or survival at the longest follow up available (35/428 [8.2%] vs. 24/433 [5.5%], RR = 1.48 [.91–2.41], p for effect = .12, p for heterogeneity = .83, I^2 = 0% [Fig. 5]).

Favorable neurologic outcome was significantly improved when considering all patients undergoing CPR (and not only the survivors): 39/307 [13%] vs. 18/293 [6%], RR = 2.35 [1.30–4.24], p for effect = .004, p for heterogeneity = .34, I^2 = 11.3% (Fig. 6).

Only one study (14) measured dioxide and oxygen saturation levels during CPR, both of which significantly improved in the ITD group.

Additional Analyses. We assessed the robustness and applicability of our findings through a series of sensitivity analyses, i.e., excluding one study at a time,

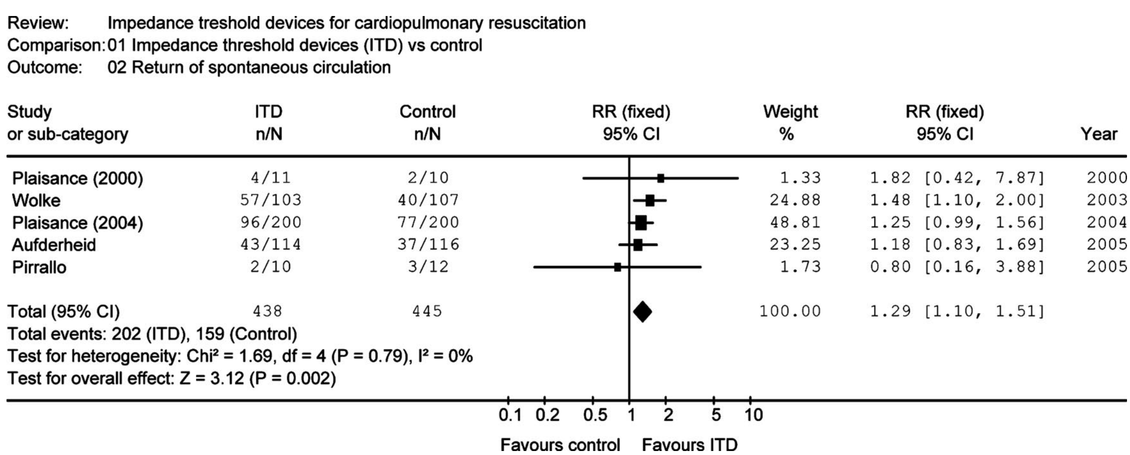

Figure 2. Forest plot for the comparison of impedance threshold devices vs. control on return of spontaneous circulation after cardiopulmonary resuscitation in five studies. *RR*, relative risk; *CI*, confidence interval.

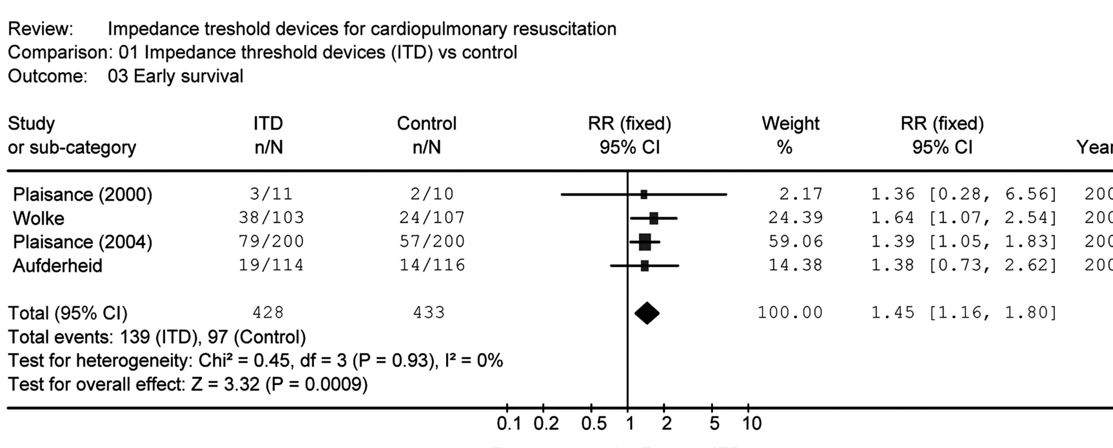

Figure 3. Forest plot for the comparison of impedance threshold devices vs. control on early survival after cardiopulmonary resuscitation in four studies. *RR*, relative risk; *CI*, confidence interval.

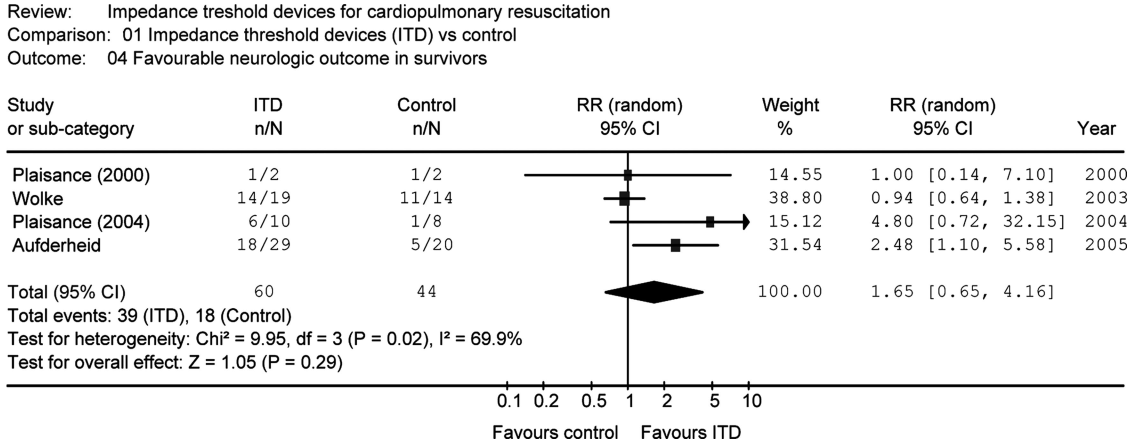

Figure 4. Forest plot for the comparison of impedance threshold devices vs. control on favorable neurologic outcome in survivors after cardiopulmonary resuscitation in four studies. *RR*, relative risk; *CI*, confidence interval.

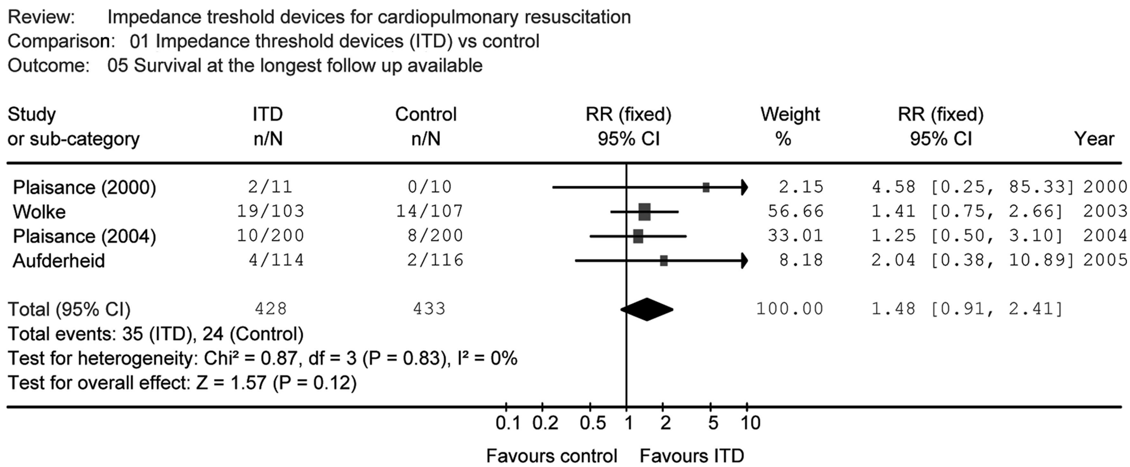

Figure 5. Forest plot for the comparison of impedance threshold devices vs. control on survival at the longest follow-up available after cardiopulmonary resuscitation in four studies. *RR*, relative risk; *CI*, confidence interval.

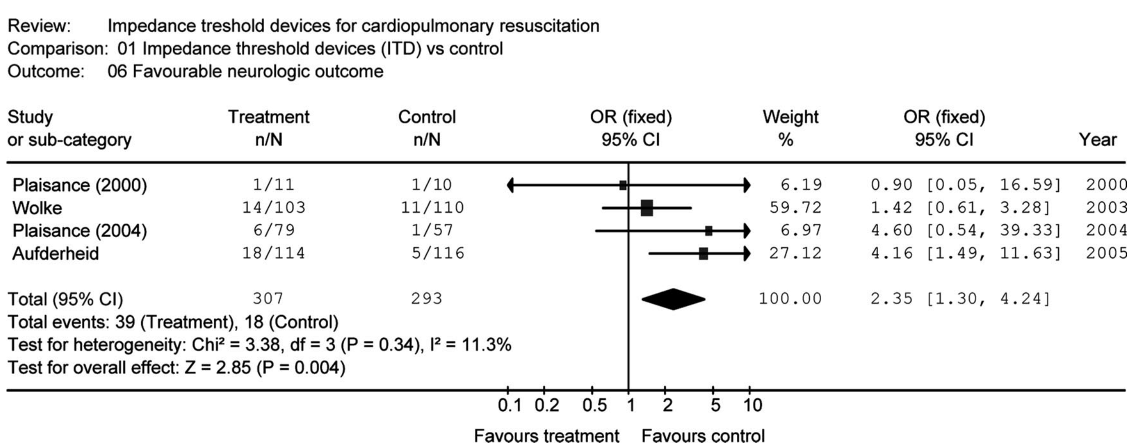

Figure 6. Forest plot for the comparison of impedence threshold devices vs. control on favorable neurologic outcome after cardiopulmonary bypass resuscitation in four studies. *OR*, odds ratio; *CI*, confidence interval.

switching from fixed-effect to random-effect models, and computing odds ratios as well as risk differences. All subanalyses were performed excluding one randomized controlled study at a time remained in the same direction and magnitude of benefit in support of ITD as the overall analysis. Similarly, random-effect meta-analyses, odds ratios, and risk differences computations confirmed the robustness of the comprehensive and primary analyses (all $p < .05$). We also appraised the robustness and validity of our findings by exploring the likelihood of small study bias by means of funnel plot inspection and Egger test (Figs. 7 and 8). Specifically, we found no major evidence of such bias either at graphical or statistical test-

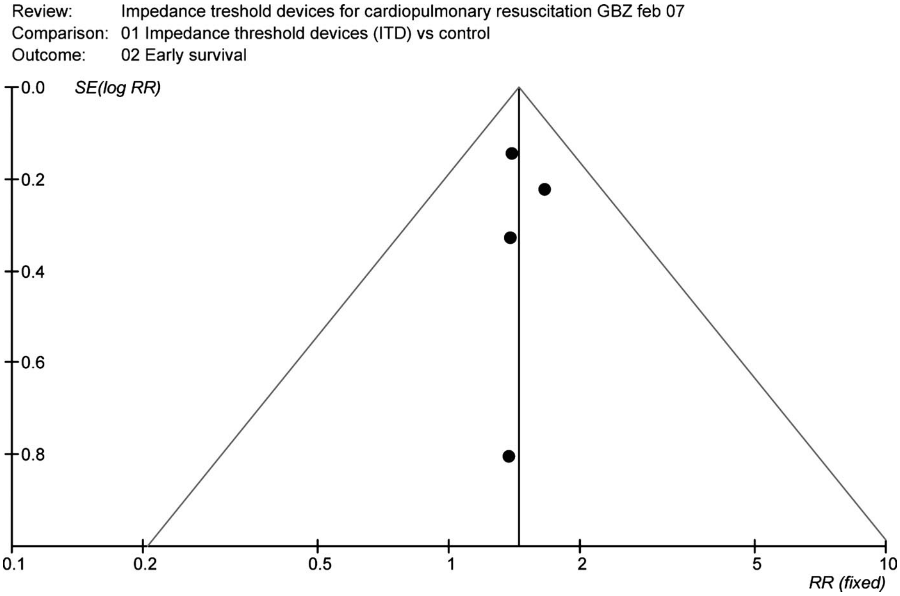

Figure 7. Funnel plot inspection and Egger test on early survival. *RR*, relative risk.

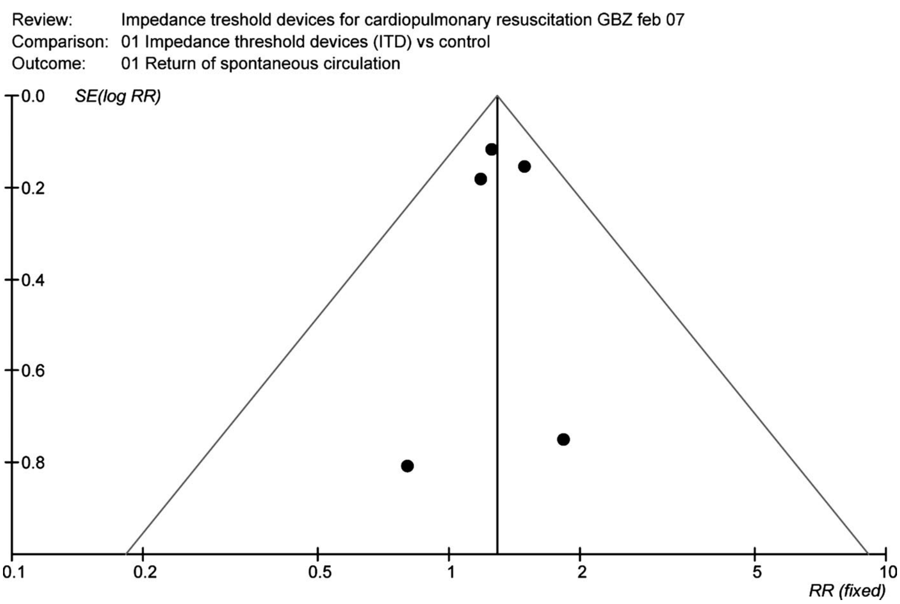

Figure 8. Funnel plot inspection and Egger test on return of spontaneous circulation. *RR*, relative risk.

ing for ROSC or early survival (*p* at Egger test, respectively, 0.90 and 0.94).

DISCUSSION

The most important result of this meta-analysis is to demonstrate that the use of ITD for cardiopulmonary resuscitation in nontraumatic out-of-hospital cardiac arrest results in significantly improved ROSC (46% vs. 36%), short term survival (32% vs. 22%), and favorable neurologic outcome in the overall population (13% vs. 6%). Although underpowered, all studies included in this analysis demonstrated positive survival trends, consistent with the overall positive results of our meta-analysis, either when used alone or combined to ACD. With this analysis we found statistically significant evidence regarding heart function recovery; probably similar results will be found for cerebral recovery function with larger studies. No systematic review regarding the efficacy of an ITD device has been published before. Unlike other CPR device studies, usually performed in an unblinded fashion, four of the five studies considered for the present review where all blinded, due to use of a sham ITD.

The findings of this meta-analysis are consistent with the hypothesis that "priming the pump" is crucial for survival after cardiac arrest (16). Survival is likely dependent on a critical blood flow to vital organs for recovery of cardiac and brain functions. The ITD causes a decrease in intrathoracic pressure and enhances venous blood return during the filling phase of the right heart. The ITD has been demonstrated to enhance vital organ perfusion and neurologically intact survival rates in animals in cardiac arrest treated with standard manual CPR (17, 18, 19, 20, 21). In two studies, (13, 14) ITD improved systemic pressure and coronary perfusion pressure when compared to standard CPR and a sham ITD or the ACD CPR and a sham ITD.

In order to optimize the benefit of the ITD, however, the rescuers must allow full recoil of the chest after each compression, lifting their palms slightly off the chest.

This CPR adjunct is very appealing since it is very easy to teach and use, and can be readily integrated in the standard of care of cardiac arrest patients and proved effective when applied to a face mask (22), hence allowing its early use even by basic life support rescue teams.

Furthermore, survival benefit was demonstrated in patients with out-of-hospital cardiac arrest with a response time often >10 mins, a group of patients traditionally considered at risk for bad outcome. The ITD extended the "window of opportunity" for successful defibrillation (15).

Other CPR adjuncts did not show such positive results: active compression-decompression devices alone were recommended with a Class IIb level only for in-hospital use in the recent American Heart Association guidelines (3). A recent review (4) found no differences in mortality between ACD-CPR and standard-CPR. It is noteworthy that the Cochrane analysis which showed no benefit from ACD CPR did not include studies in which the combination of ACD CPR + ITD was used (4). The combination of ACD plus ITD has a synergistic effect, assuring more negative intrathoracic pressure and greater venous return during the decompression phase (14). Further studies comparing standard CPR and ACD+ITD for long-term outcomes could lead to a reappraisal of ACD when used in combination with the ITD. The critical importance of training and fatigue in the performance of ACD-CPR is a well known problem (3).

It should be noted that excessive ventilation rates have been shown to be life-threatening: hyperventilation decreases venous return to the heart, decreases coronary perfusion pressure, and increases intracranial pressure (23). To address this problem, ventilation timing assist lights at a rate of 10/min were added to an improved version of ITD, so adding another positive effect to the device.

The ITD appears to have a very satisfactory safety profile: none of the studies report differences in adverse events or complications rates with ITD when compared with control groups. However, rescuers must remember to remove the device after ROSC.

ITD was first described in 1995 (5), but still needs to be properly studied in selected settings such as early CPR, in-hospital basic life support, and in CPR performed by trained medical personnel: an even higher beneficial effect has been hypothesized in this patients' population (12). There is still uncertainty in the responsiveness of specific cardiac rhythms to this device. Wolcke et al. (15) evidenced improved success rate in patients with ventricular fibrillation, while Aufderheide et al. (12) reported the best results in patients with pulseless electrical activity (at any time during CPR). Thayne et al. (24) performed a case matched study on ITD with excellent results limited to patients presenting with asystolic rhythm.

Limitations. The limitations of systematic reviews and meta-analyses are well known and include the level of uniformity among study populations as well as the primary end points in each study, (25) and the fact that negative results are always less often published. A particular limitation of our analysis is the underlying statistical inconsistency and the absence of long term outcomes. We strove nonetheless to comply with the most stringent guidelines of the Cochrane Collaboration and of the QUOROM statement. Thus our results provide the most comprehensive and thorough comparison of ITD vs. control which currently exists. It should be noted as a source of clinical heterogeneity that both the control group and treatment group care varied between trials. In particular, two trials (12, 14) estimated the effect of ITD when added to standard CPR, two trials (7, 13) estimated the effect of ITD when added to ACD-CPR, and one trial (15) compared ACD-CPR + ITD to standard CPR, making it impossible to separate the effects of ACD CPR and ITD in this trial. Nonetheless, only an individual patient-data meta-analysis or a large and adequately powered randomized controlled study could provide a sounder and more rigorous appraisal of the clinical role of ITD in this clinical setting.

The new guidelines for CPR (3) focus on more compressions and fewer ventilations to minimize the no-flow periods as much as feasible. In these scenarios, ITD could further enhance circulation or, on the contrary, it could be superfluous, its benefits being already achieved by the improved chest compressions. However, a recent study in animals treated with two different compression:ventilation ratios (15:2 vs. 30:2) in the absence and presence of the ITD suggests that the ITD is of benefit when using a reduced ventilation rate strategy (26).

CONCLUSIONS

ITD appears to improve short-term survival after nontraumatic out-of-hospital cardiac arrest. Given the limitations of meta-analysis, our analysis supports the use of ITD during standard CPR. A larger multicenter, randomized, controlled trial, following the new guidelines for CPR and with long-term follow-up will be needed to confirm these results and assess long-term outcome.

ACKNOWLEDGMENTS

This study is part of a senior training project of the "Meta-analysis and Evidence-based Medicine Training in Cardiology" (METCARDIO, formerly COMET) based in Milan, Italy (www.metcardio.org).

REFERENCES

1. Horsted TD, Rasmussen LS, Meyhoff CS, et al: Long-term prognosis after out-of-hospital cardiac arrest. *Resuscitation* 2007; 72: 214–218
2. Dunnea RB, Comptona S, Zalenski RJ, et al: Outcomes from out-of-hospital cardiac arrest in Detroit. *Resuscitation* 2007; 72:59–65
3. ECC Committee, Subcommittees and Task Forces of the American Heart Association. 2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2005; 112(suppl IV):1–203
4. Lafuente-Lafuente C, Melero-Bascones M: Active chest compression-decompression for cardiopulmonary resuscitation. Cochrane Database of Systematic Reviews 2004, Issue 4. Art. No.: CD002751. DOI: 10.1002/14651858.CD002751.pub2
5. Lurie KG, Coffeen P, Schultz J, et al: Improving active compression-decompression cardiopulmonary resuscitation with an inspiratory impedance valve. *Circulation* 1995; 91: 1629–1632
6. Lurie KG, Plaisance P, Sukhum P, et al: Mechanical advances in cardiopulmonary resuscitation. *Curr Opin Crit Care* 2001; 7:170–175
7. Plaisance P, Lurie KG, Vicaut E, et al: Evaluation of an impedance threshold device in patients receiving active compression-decompression cardiopulmonary resuscitation for out of hospital cardiac arrest. *Resuscitation* 2004; 61:265–271
8. Fleiss JL: The statistical basis of meta-analysis. *Stat Methods Med Res* 1993; 2:121–145
9. Higgins JP, Thompson SG, Deeks JJ, et al: Measuring inconsistency in meta-analyses. *BMJ* 2003; 327:557–560
10. Egger M, Davey Smith G, et al: Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997; 315:629–634
11. Higgins JPT, Green S. The Cochrane Handbook for Systematic Reviews of Interventions 4.2.5. Available at: http://www.cochrane.org/resources/handbook/hbook.htm. Accessed 10 April 2007
12. Aufderheide TP, Pirrallo RG, Provo TA, et al: Clinical evaluation of an inspiratory impedance threshold device during standard cardiopulmonary resuscitation in patients with out-of-hospital cardiac arrest. *Crit Care Med* 2005; 33:734–740
13. Plaisance P, Lurie KG, Payen D: Inspiratory impedance during active compression-decompression cardiopulmonary resuscitation: a randomized evaluation in patients in cardiac arrest. *Circulation* 2000; 101:989–994
14. Pirrallo RG, Aufderheide TP, Provo TA, et al: Effect of an inspiratory impedance threshold device on hemodynamics during conventional manual cardiopulmonary resuscitation. *Resuscitation* 2005; 66:13–20
15. Wolcke BB, Mauer DK, Schoefmann MF, et al: Comparison of standard cardiopulmonary resuscitation versus the combination of active compression-decompression cardiopulmonary resuscitation and an inspiratory impedance threshold device for out-of-hospital cardiac arrest. *Circulation* 2003; 108: 2201–2205
16. Wik L, Hansen TB, Fylling F, et al: Dalaying defibrillation to give basic cardiopulmonary resuscitation to patients with out-of-hospital ventricular fibrillation: a randomised trial. *JAMA* 2003; 289:1389–1395
17. Lurie KG, Voelckel WG, Zielinski T, et al: Improving standard cardiopulmonary resuscitation with an inspiratory impedance threshold valve in a porcine model of cardiac arrest. *Anesth Analg* 2001; 93:649–655
18. Lurie KG, Zielinski T, McKnite S, et al: Use of an inspiratory impedance valve improves neurologically intact survival in a porcine model of ventricular fibrillation. *Circulation* 2002; 105:124–129
19. Voelckel W, Lurie KG, Sweeney M, et al: Effect of active compression-decompression cardiopulmonary resuscitation with the im-

pedance threshold valve in a young porcine model of cardiac arrest. *Pediatric Res* 2002; 51:523–527
20. Langhelle A, Stromme T, Sunde K, et al: Inspiratory impedance threshold device cardiopulmonary resuscitation. *Resuscitation* 2002; 52:39–48
21. Lurie KG, Mulligan KA, McKnite S, et al: Optimizing standard cardiopulmonary resuscitation with an inspiratory impedance threshold device. *Chest* 1998;113:1084–1090
22. Plaisance P, Soleil C, Lurie KG, et al: Use of an inspiratory impedance threshold device on a face mask and endotracheal tube to reduce intrathoracic pressures during the decompression phase of active compression-decompression cardiopulmonary resuscitation. *Crit Care Med* 2005; 33: 990–994
23. Aufderheide TP, Sigurdsson G, Pirrallo RG, et al: Hyperventilation induced hypotension during cardiopulmonary resuscitation. *Circulation* 2004; 109:1960–1965
24. Thayne RC, Thomas DC, Neville JD, et al: Use of an impedance threshold device improves short-term outcomes following out-of-hospital cardiac arrest. *Resuscitation* 2005; 67:103–108
25. Biondi-Zoccai GG, Agostoni P, Abbate A: Parallel hierarchy of scientific studies in cardiovascular medicine. *Ital Heart J* 2003; 4:819–820
26. Yannopoulos D, Aufderheide TP, Gabrielli A, et al: Clinical and hemodynamic comparison of 15:2 and 30:2 compression-to-ventilation ratios for cardiopulmonary resuscitation. *Crit Care Med* 2006; 34:1444–1449

APPENDIX

BioMedCentral was searched according to the following strategy (yielding 25 citations): *impedance AND threshold AND device AND (random* OR control*)*

CENTRAL was searched according to the following strategy (yielding 1 citation): (*(impedance) and (threshold) and device)*) *or itd*

PubMed was searched according to the following strategy (yielding 17 citations): Biondi-zoccai et al. int j epidemiol

((impedance AND threshold AND device) OR itd) AND (resuscitation OR ((cardiac OR cardiopulmonary) AND arrest)) AND (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized controlled trials[mh] OR random allocation[mh] OR double-blind method[mh] OR single-blind method[mh] OR clinical trial[pt] OR clinical trials[mh] OR (clinical trial[tw] OR ((singl[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask*[tw] OR blind[tw])) OR (latin square[tw]) OR placebos[mh] OR placebo*[tw] OR random*[tw] OR research design[mh:noexp] OR evaluation studies[mh] OR follow-up studies[mh] OR prospective studies[mh] OR crossover studies[mh] OR control*[tw] OR prospectiv*[tw] OR volunteer*[tw]) NOT (animal[mh] NOT human[mh]) NOT (comment[pt] OR editorial[pt] OR meta-analysis[pt] OR practice-guideline[pt] OR review[pt]))*