WORKSHEET for Evidence-Based Review of Science for Veterinary CPCR

1. Basic Demographics

Worksheet author(s)

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[redacted]

2. Clinical question:

In intubated dogs and cats with cardiac arrest (P), does the use of an impedance threshold device (I), as opposed to routine CPR without an impedance valve (C), improve outcome (O) (e.g. ROSC, survival)?

3. Conflict of interest specific to this question:

None

4. Search strategy (including electronic databases searched):

4a. Databases

Medline via PubMed (1998 - May 2011)

Keywords:

1. Cardiopulmonary Resuscitation
2. Impedance Threshold Device
3. ITD
4. ResQPod
5. ResQGuard

Results for 2 alone: 580; only 31 relevant
Results for 1 and 2: 48; only 31 relevant
Results for 1 and 3: 24; only 19 relevant
Results for 1 and 4: 0
Results for 1 and 5: 0

4b. Other sources

Hand searching medical journals revealed no additional references and cross referencing all initial references with references from American Heart and Lung Association CPR Guidelines 2010 revealed 4 additional references

Of the relevant articles found, 20 included for review.

4c. State inclusion and exclusion criteria for choosing studies and list number of studies excluded per criterion

Inclusion criteria

Clinical studies (randomized, controlled) involving human, porcine, canine, feline subjects where by an impedance threshold device was used during cardiopulmonary arrest were included.

Exclusion criteria

Impedance threshold devices used in clinical studies for the treatment of cardiogenic shock and hypotension were excluded. Review articles, meta-analysis, case studies, and case series were excluded. Studies involving species other than human, porcine, feline, canine were excluded.

4d. Number of articles/sources meeting criteria for further review:

20

5. Summary of evidence

Evidence Supporting Clinical Question

Good						*Pirrallo 2005 E* *Plaisance 2002 A* *Plaisance 2004 AB*
Fair						*Aufderheide 2005 ABE* *Plaisnace 2005 E* *Lurie 2001 E* *Lurie 2002 ABCD* *Thayne 2005 AB* *Yannopoulos 2005 AB* *Yannopoulos2004 and 2006 E*
Poor						*Babbs 2005 E* *Lurie 1998 E* *Raedler 2000 E* *Wolcke 2003 AB* *Yannopoulos 2006 AE*
	1	**2**	**3**	**4**	**5**	**6**
Level of evidence (P)						

A = Return of spontaneous circulation
B = Survival of event
C = Survival to hospital discharge
D = Intact neurological survival
E = Other endpoint
Italics = Non-target species studies

Evidence Neutral to Clinical question

Good						
Fair						
Poor						
	1	**2**	**3**	**4**	**5**	**6**
Level of evidence (P)						

A = Return of spontaneous circulation
B = Survival of event
C = Survival to hospital discharge
D = Intact neurological survival
E = Other endpoint
Italics = Non-target species studies

Evidence Opposing Clinical Question

Good						*Mader 2008 AB*
Fair						
Poor						*Menegazzi 2007 AB* *Herff 2007 E*
	1	**2**	**3**	**4**	**5**	**6**
Level of evidence (P)						

A = Return of spontaneous circulation
B = Survival of event
C = Survival to hospital discharge
D = Intact neurological survival
E = Other endpoint
Italics = Non-target species studies

6. REVIEWER'S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

No veterinary prospective studies exist regarding use of an impedance threshold device (ITD). Improvements in venous return as a result of negative intrathoracic pressure plateaus at -10cmH2O in a computerized model (2), and as a result, commercial devices to augment intrathoracic pressure during manual ventilation have been researched and developed. Intrathoracic pressure is most negative in human cardiopulmonary arrest (CPA) subjects when intubated (compared to face mask) and when an ITD is used (12). Numerous porcine prospective studies have demonstrated improved carotid blood flow, cerebral perfusion, and coronary perfusion with the use of an ITD to augment ventilation and venous return (1,4-7,13,17-20). Other studies involving porcine subjects also demonstrated improvements in end-tidal-carbon dioxide (ETCO2) with use of an ITD (6,7,10,17,18,20). Despite these improvements in vital organ perfusion and ETCO2, results of these porcine models of CPA have been mixed with respect to return of spontaneous circulation (ROSC), with no difference in two studies (5, 20) and improved ROSC in four studies (6,14,17,18). Of these four porcine studies, two showed not only improved ROSC, but also improved survival (6,14). The latter study unfortunately is confounded by more than one intervention (14). Of note was Lurie's 2002 study (6) which also showed improved neurologic outcome when ETCO2 was >18mmHg. Contrasting these results, were two studies (7,8) which did not show any improvements in vital organ perfusion, ROSC or survival. The latter study however was underpowered and not blinded (8).

The convincing nature of these initial studies using a porcine model of CPA, which was typically conducted by inducing ventricular fibrillation, prompted some prospective work on humans experiencing out-of-hospital cardiopulmonary arrest. These studies did include multiple arrest rhythms, making them a better model of CPA. Of great importance is the fact that none of the human prospective CPR studies using an ITD showed any significant adverse events or complications. Most did show improvements in ROSC (10, 15) and 24-hour survival time (1,11,16), and those that did not, did document improved vital organ perfusion (9, 17). Wolcke's study, though convincing, did have some confounding factors as more than one intervention was studied (16). No human CPR studies showed improved long term survival with use of an ITD (1,9,10,11,15-17).

7. Conclusion

There are no clinical veterinary studies or reports on use of an ITD in CPA in dogs or cats. There is convincing evidence in porcine and human CPA-ITD studies which support its use. The evidence indicates that an ITD may be useful for initial resuscitation efforts in cases of cardiopulmonary arrest in veterinary patients. All clinical data in human CPA-ITD studies have involved adult CPR recommendations (adult defined as at least 8-12 years of age). As such, the manufacturer of the commercially available ITD recommends its use in CPA when adult basic life support and CPR is employed, and there is no current recommendation for pediatrics or neonates. This reflects a lack of research in pediatric CPR-ITD studies. The commercially available ResQPod does add 40.7ml of dead space, and this may be a limitation of this device in very small patients. As many veterinary patients have cardiac arrest secondary to respiratory arrest, care should be taken to ensure these patients are adequately ventilated according to current compression-ventilation ratio protocol with 100% oxygen. Contraindications of ITD use involve severe chest trauma causing flail chest, open chest wound, and large diaphragmatic defect (which would result in loss of negative intrathoracic pressure), and ongoing severe hemorrhage (ITD use may promote further blood loss).

9. Citation list

1. Clinical evaluation of an inspiratory impedance threshold device during standard cardiopulmonary resuscitation in patients with out-of-hospital cardiac arrest
Aufderheide et al, *CCM* 2005;33(1):734-740
Study design: prospective, randomized, double-blinded, intention-to-treat study of out of hospital CPA with standard CPR with sham-ITD or ITD. Overall ICU admission did not differ between groups; however, PEA subgroup had higher ICU admission. NO diff 24 hour survival. Post-hoc analysis of patients with PEA *at any time* had significantly higher ICU admission and 24 hour survival time. NO statically significant differences for vfib and asystole cohort. No differences in adverse events or complications. This study was underpowered.

2. A dose—response curve for the negative bias pressure of an intrathoracic pressure regulator during CPR
Babbs et al, *Resuscitation* 2005;71(1): 365-368
Study design: computerized model to determine the ideal negative intrathoracic pressure needed to augment venous return. Perfusion pressure increases 50% at a -10cmH20 airway pressure, and levels lower than -10cmH20 do not further contribute to enhanced perfusion pressure.

3. Use of an inspiratory impedance threshold valve during chest compressions without assisted ventilation may result in hypoxemia.
Herff et al, *Resuscitation* 2007;72(3):466-476
Study design: prospective, cross over porcine study of how an ITD affects oxygenation. Study animals were alive and anesthetized, and not ventilated. Use of an ITD without ventilation resulted in SpO2 readings of <70% within 126 seconds. This study used a ITD with a cracking pressure of 35cmH2O rather than the standard 10cmH20

4. Optimizing standard cardiopulmonary resuscitation with an impedance threshold valve.
Lurie et al, *Chest* 1998;113(4):1084-1090
Study design: prospective cross over porcine study. Improved cerebral and coronary perfusion. The valve used in this study had a -40cmH20 cracking pressure.

5. Improving standard cardiopulmonary resuscitation with an inspiratory impedance threshold valve in a porcine model of cardiac arrest. Lurie et al, *Anesthesia and Analgesia* 2001;93(3):649-655
Study design: prospective, randomized, double blinded porcine trial of standard CPR with or without an ITD. Significantly higher coronary and cerebral perfusion at 2 min. No difference in ROSC.

6. Use of an impedance threshold valve improves neurologically intact survival in a porcine model of ventricular fibrillation.
Lurie et al, *Circulation* 2002;105(1):124-129
Study design: prospective, randomized, double blinded porcine study of standard CPR with an ITD or without (sham). Significantly more survivors at 24 hours in the ITD group, with higher ETCO2, with a value of >18 correlating to survival, and those had significantly higher neurologic scores.

7. A blinded, randomized controlled evaluation of an impedance threshold device during cardiopulmonary resuscitation in swine
Mader et al, *Resuscitation* 2008;77:387-394
Study design: prospective, randomized, double blinded study porcine study of induced CPA and CPR with or without and ITD. Mean CPP, PaCO2, PaO2, BE, ROSC and 20min survival did not differ between groups.

8. Effects of an impedance threshold device on hemodynamics and restoration of spontaneous circulation in prolonged porcine ventricular fibrillation.
Menegazzi JJ et al. *Prehosp Emerg Care* 2007;11(2):179-85.
Study design: prospective randomized porcine trial of standard CPR versus CPR with an ITD. Significantly lower ROSC and 24 hour survival with use of the ITD. Underpowered study. Not blinded.

9. Effect of an inspiratory impedance threshold device on hemodynamics during conventional manual cardiopulmonary resuscitation
Pirrallo et al, *Resuscitation* 2005;66(1):13-20
Study design: prospective, randomized, double-blind, intention-to-treat study of out of hospital CPA in human subjects. N=22 randomized patients. Direct arterial blood pressure measures with ITD CPR versus shamITD-CPR were significantly higher at 2, 5, and 7min post initiation of CPR efforts. No other significant differences between Sham-ITD and ITD groups (including arrest rhythm, PEA, asystole and vfib). No adverse events or complications.

10. Inspiratory impedance during active compression-decompression cardiopulmonary resuscitation: a randomized evaluation in patients in cardiac arrest
Plaisance et al, *Circulation* 2002;101(9):989-994
Study design: prospective, randomized, blinded trial of out of hospital cardiac arrest patients and use of ACD CPR with ITD. Trauma cases were excluded. Use of ITD allowed significantly higher ETCO2, coronary perfusion, diastolic pressure, and ROSC. Study was underpowered for survival analysis. All patients had asystole. No vfib patients.

11. Evaluation of an impedance threshold device in patients receiving active compression–decompression cardiopulmonary resuscitation for out of hospital cardiac arrest
Plaisance et al, *Resuscitation* 2004;61(3):265-271
Study design: prospective, multicenter, randomized, blinded
Active compression-decompression CPR with ITD compared to sham device had significantly higher ROSC, ICU admission, and 24 hours survival for out of hospital CPA, however, survival to hospital discharge was not significantly different. All three arrest rhythms represented in this study (asystole 74%, 23% vfib, 3%PEA).

12. 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.
Plaisance P, Soleil C, Lurie KG, Vicaut E, Ducros L, Payen D.
CCM 2005 May;33(5):990-4.
Study design: prospective, randomized, blinded, crossover of standard CPR with or without an ITD. Mean negative intrathoracic pressure was greater with use of an ITD, and was lowest when patients were ventilated with an endotracheal tube versus a face mask.

13. Vasopressor response in a porcine model of hypothermic cardiac arrest is improved with active compression-decompression cardiopulmonary resuscitation using the inspiratory impedance threshold valve.
Raedler et al, *Anesthesia and Analgesia* 2000;95(6):1496-1502
Study design: prospective randomized trial of a porcine model of CPA comparing standard CPR with vasopressin to ACD-CPR with vasopressin and ITD device. The ACD-CPR-ITD group had significantly higher carotid artery blood flow and coronary perfusion.

14. Rapid Induction of Cerebral Hypothermia Is Enhanced With Active Compression-Decompression Plus Inspiratory Impedance Threshold Device Cardiopulmonary Resuscitation in a Porcine Model of Cardiac Arrest
Srinivasan et al. *Journal of the American College of Cardiology*; 47(4):835-841
Study design: prospective, randomized porcine study of standard CPR versus ACD-CPR with ITD AND active cooling which was initiated 2min after CPR efforts. Brain tissue was significantly cooler in the ACD-CPR and ITD group compared to standard CPR group. Significantly more pigs survived in the ACD-CPR and ITD group versus the standard, and the ACD-group with ITD had higher coronary perfusion, and lower atrial pressures. Confounded by two interventions.

15. Use of an impedance threshold device improves short-term outcomes following out –of-hospital cardiac arrest.
Thayne et al, *Resuscitation* 2005;67(1):103-108
Study design: prospective study with historical matched-case controls of out-of-hospital cardiac arrest. Use of ITD had significantly higher emergency department admission compared to matched controls. Subgroup analysis of patients with asystole had three times the survival to admission the emergency department.

16. 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
Wolcke et al, *Circulation* 2003;108(18):2201-5
Study design: prospective out of hospital CPR study with conventional CPR versus active compression-decompression CPR WITH an ITD. ACD-CPR with ITD had significantly higher ROSC, 1 hr survival and 24 hr survival. For witnessed arrests, 1 hr survival and 24 hr survival were significantly higher. For patients of CPA >10min (not witnessed) had significantly higher 1 hr survival. Survival to discharge was not different between ACD-CPR with ITD vs. standard CPR. No significant complications or adverse events. Confounded by two different interventions.

17. Clinical and hemodynamic comparison of 15:2 and 30:2 compression-to-ventilation ratios for cardiopulmonary resuscitation
Yannopoulos et al, *CCM* 2006;34(5):1444-9
Study design: prospective, randomized porcine study of CPR using 15:2 or 30:2 compression to ventilation ratio, AND with or without use of an ITD (ITD added 6min after initial CPR). The higher compression to ventilation (C:V) ratio of 30:2 had significantly higher: diastolic blood pressure, coronary perfusion pressure, cerebral perfusion pressure, carotid artery blood flow, end tidal CO2, and mixed venous O2. The 30:2 ratio allowed for a lower 'no compression time' and greater number of compressions. For the 30:2 C:V group, use of ITD had significantly higher diastolic blood pressure and mean arterial pressure, coronary perfusion pressure, cerebral perfusion pressure, and lower diastolic right atrial pressure. Compression number was not different between the ITD group and non-ITD group. Systolic arterial blood pressure and cardiac output were not different. Significantly higher ROSC with the 30:2 with ITD versus 15:2 with ITD groups. CPA was induced by vfib.

18. Intrathoracic Pressure Regulator During Continuous-Chest-Compression Advanced Cardiac Resuscitation Improves Vital Organ Perfusion Pressures in a
Porcine Model of Cardiac Arrest
Yannopoulos et al, *Circulation* 2005;Aug(9):803-811

Study design: prospective, randomized porcine trial comparing standard CPR to ITD-CPR. Statistically significant improvements in perfusion parameters, end tidal CO2, and one hour survival when the ITD was used. Significantly lower pH, lower PaO2, higher PaCO2, higher ETCO2 and lower vital volumes when ITD is used.

19. Reducing ventilation frequency combined with an inspiratory impedance device improves CPR efficiency in swine model of cardiac arrest
Yannopoulos et al, *Resuscitation* 2004;61:75-82
Study design: prospective, randomized porcine study. Significantly improved vital organ perfusion when an ITD was used.

20. Hemodynamic and respiratory effects of negative tracheal pressure during CPR in pigs
Yannopoulos et al, *Resuscitation* 2006;69:487-494
Study design: prospective, randomized porcine trial of standard CPR and CPR with an ITD. Use of an ITD resulted in significantly lower diastolic right atrial pressure, mean arterial pressure, cerebral and coronary perfusion pressure, and higher ETCO2. Mean arterial pH was lower in the ITD group, and arterial PCO2 and PO2 were higher. No differences in ROSC.