BACKGROUND

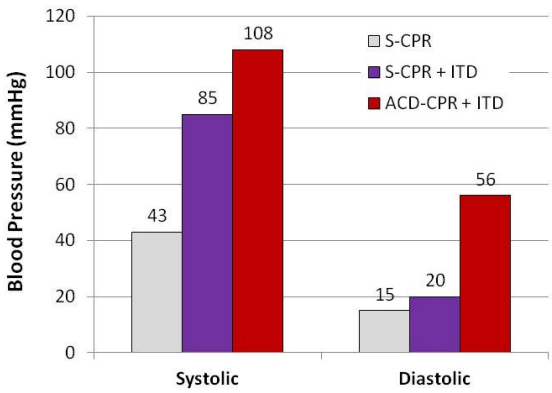
Even when performed correctly, conventional, manual, standard cardiopulmonary resuscitation (S-CPR) provides only 10 – 20% of normal blood flow to the heart, and 20 – 30% of normal blood flow to the brain. This is partially due to the fact that conventional CPR is inherently inefficient for two reasons:

1. Filling of the heart (preload) is dependent upon the chest wall's ability to passively recoil. Inadequate chest wall recoil can occur if: a) the chest is not very compliant, b) rescuers tire and begin to "rest" on the chest, or c) ribs are broken.
2. With an open airway, as the chest wall recoils, air is drawn in and wipes out the vacuum (negative intrathoracic pressure) that is responsible for creating preload.

A device (**ResQPUMP, CardioPump**) that performs active compression decompression CPR (ACD-CPR) **addresses the first inefficiency** as it assures that the chest wall is actively re-expanded and begins the creation of the all-important vacuum.

An impedance threshold device (**ResQPOD ITD**) **corrects the second inefficiency** as it selectively prevents unnecessary air from being drawn into chest during the recoil phase of CPR, thus enhancing the vacuum.

Figure 1



The devices work synergistically together. The ResQPOD "activates" the thoracic pump mechanism, while the ResQPUMP "accelerates" the therapeutic effect. The combination of adding an ITD to ACD-CPR has been shown in animal studies to improve vital organ blood flow during cardiac arrest compared to either device individually; and compared to standard CPR, ACD-CPR with an ITD has demonstrated a four-fold improvement in blood flow to the heart, and a more than doubling of blood flow to the brain.[1] As shown in Figure 1, the device combination has also been shown in human studies to provide near-normal systolic and diastolic blood pressures during cardiac arrest.[2,3]

In addition, adding an ITD to ACD-CPR has been shown to improve short-term (24-hour) survival in patients in cardiac arrest compared to both S-CPR (Figure 2),[4] and ACD-CPR (Figure 3)[5] alone:

Figure 2

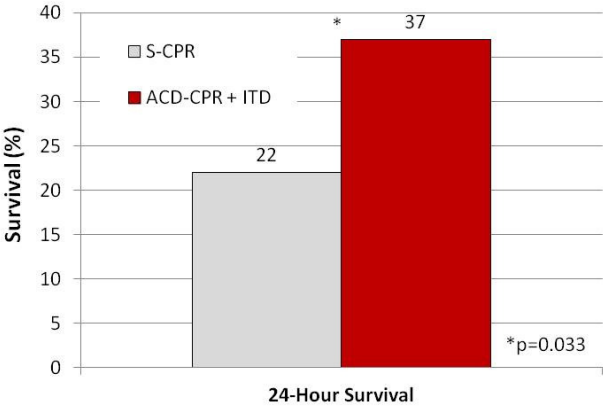
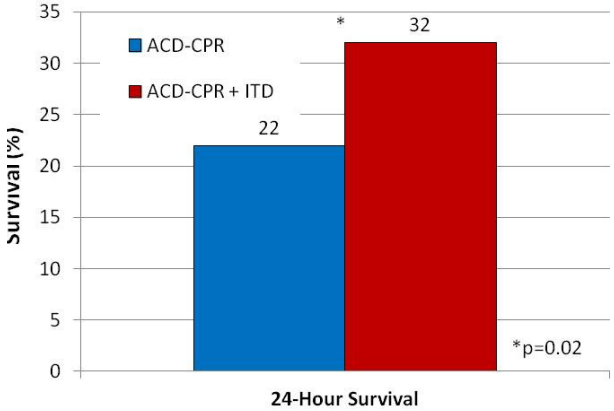


Figure 3



PURPOSE

The purpose of the ResQTRIAL was to evaluate the safety and long-term survival benefit of patients receiving ACD-CPR with an ITD during out-of-hospital, non-traumatic cardiac arrest.[6]

METHODS/STUDY DESIGN

- Prospective, randomized, multi-center, blinded (during follow-up) 2-arm trial comparing:

Control Group

Figure 4. Conventional, manual CPR (S-CPR), performed with a pair of hands

Intervention Group

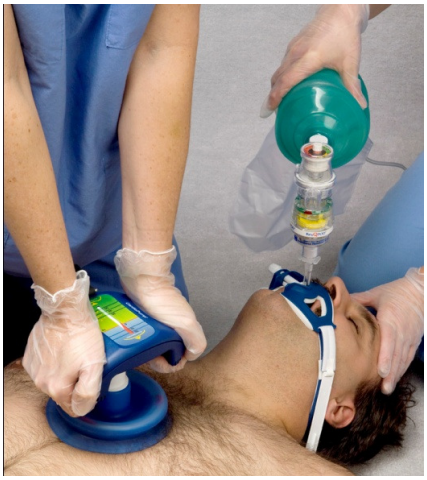


Figure 5. ACD-CPR (performed with the ResQPUMP) and an ITD (ResQPOD)

The only variable studied was the method of CPR performed by emergency medical services (EMS) personnel. Strong emphasis was placed on immediate chest compressions with early placement of both study devices. All other aspects of patient care (e.g. IV therapy, medications, defibrillation) were similar between the two groups. Rescuers, investigators and the sponsor were all blinded to CPR method during patient follow-up and to aggregate study results during the conduct of the trial.

STUDY DEVICES

Figure 6. ResQPUMP® ACD-CPR Device:

The ResQPUMP is a hand-held device placed in the same position on the sternum as hands are for S-CPR (mid-nipple line on the lower half of sternum). It allows rescuers to perform a similar chest compression (to a depth of 2”), but instead of relying on the chest wall to recoil passively, rescuers pull up on the handle with the suction cup and provide active decompression of the chest, thereby assuring proper chest wall recoil and the creation of a vacuum (negative intrathoracic pressure) that helps return blood to the heart. The handle contains a force gauge and metronome that guide compression depth, recoil and rate (80/min). It is identical to the CardioPump®, which is CE marked and currently marketed outside the United States (US). Use of the ResQPUMP is considered investigational in the US. Both the ResQPUMP and the CardioPump are manufactured by Advanced Circulatory Systems Inc (ACSI).

Figure 7. ResQPOD Impedance Threshold Device:

The ResQPOD® is an ITD that selectively prevents unnecessary respiratory gases from the entering the chest during the chest wall recoil phase of CPR. It is attached within the ventilation circuit, between the airway adjunct (e.g. facemask, ET tube) and the ventilation source (e.g. ventilation bag). By selectively impeding airflow during CPR, it optimizes the intrathoracic vacuum that is generated during chest wall recoil, thereby increasing preload, and thus, cardiac output on the subsequent compression. There is no significant resistance to patient exhalation or rescuer ventilation. Timing assist lights help guide rescuers to ventilate at the proper rate. The ResQPOD is commercially available in the US (-10 cmH_20 inspiratory impedance) and outside the US (-16 cmH_20 inspiratory impedance[a]). The ResQPOD is manufactured by ACSI.

STUDY ENDPOINTS

Primary Endpoint:

Survival to hospital discharge with favorable neurologic function, defined as a modified Rankin Scale (mRS) score ≤ 3.

Secondary Endpoints:

- Adverse event rates (e.g. death, rib fractures, organ injury, etc.) through hospital discharge
- Return of spontaneous circulation
- Survival to hospital admission
- Survival to 24 hours
- Survival to and neurologic function at hospital discharge
- Survival to and neurologic function at 30 days
- Survival to and neurologic function at 90 days
- Survival to and neurologic function at one year

Neurologic Assessments Performed on Survivors:

1. Modified Rankin Scale (mRS)
2. Cerebral Performance Category (CPC)
3. Overall Performance Category (OPC)
4. Health Utilities Index 3
5. Disability Rating Scale
6. Cognitive Abilities Screening Instrument
7. Trail-Making Test
8. Beck Depression Inventory II
9. Mayo-Portland Adaptability Inventory-4
10. Quality of Life Survey

STUDY ENROLLMENT CRITERIA

Inclusion Criteria:

- Adults ≥ 18 years of age
- Subjects with presumed non-traumatic, out-of-hospital cardiac arrest
- Subjects who received at least one minute of EMS CPR

Exclusion Criteria:

- Subjects < 18 years of age
- Subjects with obvious or likely traumatic injuries causing cardiac arrest
- Subjects with pre-existing DNR orders or signs of obvious clinical death
- Subjects whose family or legal guardians requested that the subject not be entered in the study
- Subjects experiencing in-hospital cardiac arrest
- Recent sternotomy (wound not appearing completely healed)
- Subjects who could not be ventilated with a facemask or advanced airway
- Subjects receiving less than one minute of CPR

STUDY SITES

The multi-center study was conducted at seven sites that included 46 EMS agencies in urban, suburban, and rural areas, and a combined total population of 2.3 million. The study protocol was reviewed and approved by 25 participating hospital institutional review boards.

Site 01 – St. Paul, Minnesota
Principal Investigator: R. J. Frascone, MD (Regions Hospital EMS)
Agencies: St. Paul Fire Department

Site 02 – Minneapolis, Minnesota
Principal Investigator: Brian Mahoney, MD (Hennepin County EMS)
Agencies: Hennepin County Ambulance, Minneapolis Fire Department and North Memorial Ambulance

Site 03 – Whatcom County, Washington
Principal Investigator: Marvin Wayne, MD (Whatcom County EMS)
Agencies: Bellingham Fire Department, Whatcom County EMS

Site 04 – Oakland and Macomb Counties, Michigan
Principal Investigator: Robert Swor, DO (Beaumont Hospital)
Agencies: Alliance Mobile Health, Birmingham Fire Department, Ferndale Fire Department, Royal Oak Fire Department and Sterling Heights Fire Department

Site 05 – Oshkosh, Wisconsin
Principal Investigator: Tom Aufderheide, MD (Medical College of Wisconsin)
Agencies: Oshkosh FD

Site 06 – Washtenaw and Livingston Counties, Michigan
Principal Investigator: Bob Domeier, MD (St. Joseph Hospital)
Agencies: Numerous ambulance services and fire departments within Washtenaw and Livingston counties

Site 07 – Indianapolis, Indiana
Principal Investigator: Michael Olinger, MD (Wishard Hospital)
Agencies: Indianapolis Fire Department, Speedway Fire Department, Carmel Fire Department and Wishard Ambulance

STUDY TIMELINE

This study enrolled its first subject in October 2005. The last subject was enrolled in July 2009 and the last survivor was followed until July 2010, when the trial officially ended.

RESULTS

- 2470 subjects were randomized and received CPR with one of the two CPR methods.
- 1653 subjects met final criteria: 813 in the control group and 840 in the intervention group.
- The control and intervention groups were similarly matched (Table 1):

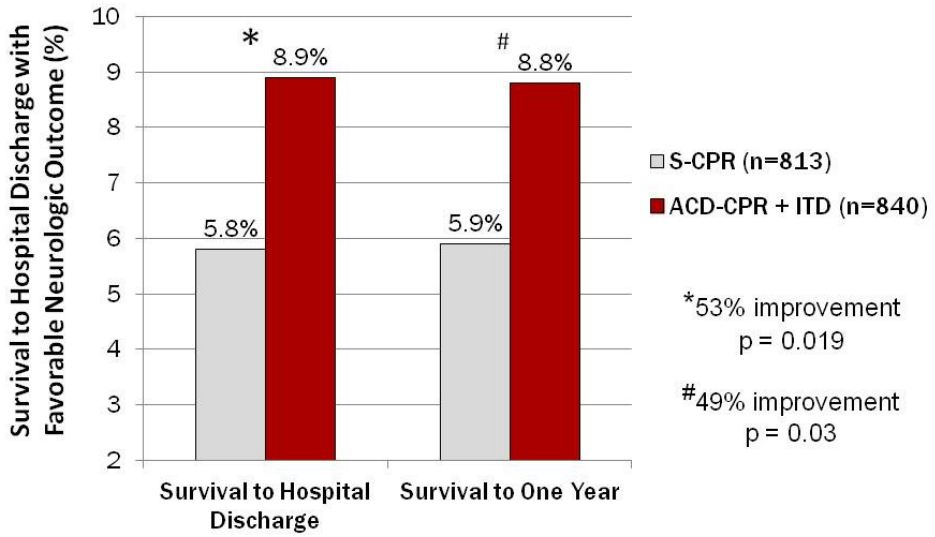
Table 1. Baseline Characteristics of Study Subjects

	Control (N = 813)	Intervention (N = 840)
Age ± SD (years)	66.8 ± 14.5	67.0 ± 15.2
Males; n (%)	539 (66.3)	558 (66.4)
Witnessed arrest; n (%)	459 (56.5)	478 (56.9)
Bystander CPR; n (%)	350 (43.1)	357 (42.5)
911 to EMS CPR ± SD (min)	6.6 ± 3.4	6.7 ± 3.2
911 to Device Placement (min)	N/A	7.1
First recorded rhythm; n (%)		
VF/pulseless VT	247 (30.4)	292 (34.8)
Asystole	379 (46.6)	375 (44.7)
PEA	180 (22.1)	170 (20.2)

Primary Endpoint and Long-Term Benefit:

Compared to the control group (S-CPR), patients in the intervention group (ACD-CPR + ITD) had a 53% relative increase in survival to hospital discharge with a Modified Rankin Scale score of ≤3. Also, patients who received the device combination had a 49% relative increase in survival to one year and both groups had similar good neurologic outcomes (Figure 8).[6]

Figure 8



In addition, the device combination was found to be helpful in cardiac arrests from a variety of non-traumatic etiologies, as well as being cardio- and neuroprotective when used with or without therapeutic hypothermia. See Figures 9 – 11.

Figure 9. Survival From Cardiac Arrest of Non-Traumatic Etiologies:

While the primary endpoint evaluated cardiac arrests from cardiac etiology, a pre-planned analysis of patients experiencing cardiac arrest from a variety of non-traumatic etiologies (e.g. respiratory, cardiac, metabolic imbalance, overdose) was also performed. This analysis found that those patients who received ACD-CPR plus an ITD had a 39% improvement in survival to hospital discharge with favorable neurologic outcome.[7]

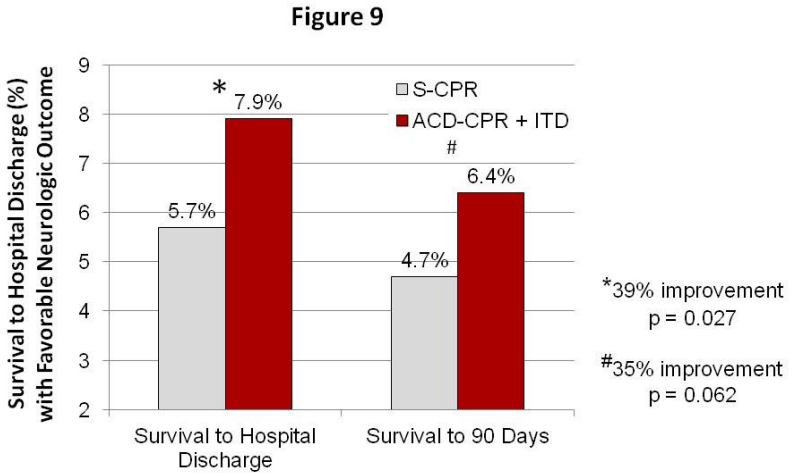


Figure 10. Neuro-Protective Benefits WITH Hypothermia

Therapeutic hypothermia was provided to some, but not all, of the patients who survived in the ResQTRIAL. For those patients who DID receive therapeutic hypothermia and ACD-CPR plus an ITD, there was a six-fold improvement (11.1% to 69.2%) in the percentage of patients who improved from poor neurologic status at hospital discharge to favorable neurologic status at 90 days, compared to those patients who received S-CPR with therapeutic hypothermia.[8]

NOTE: Poor neurologic status defined as Cerebral Performance Category (CPC) of ≥3; favorable neurologic status defined as CPC of 1 or 2.

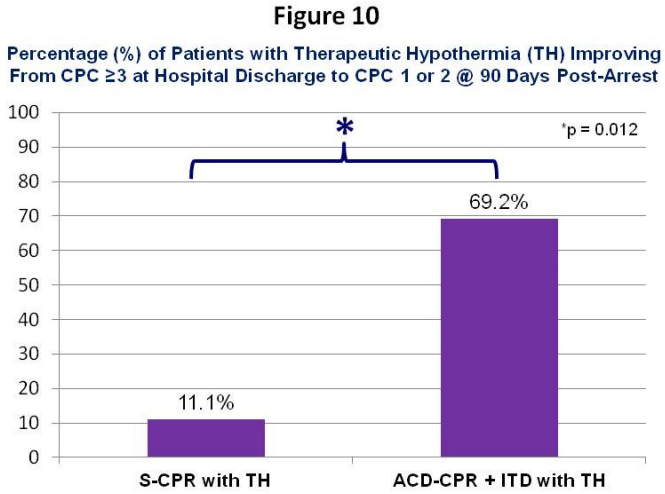
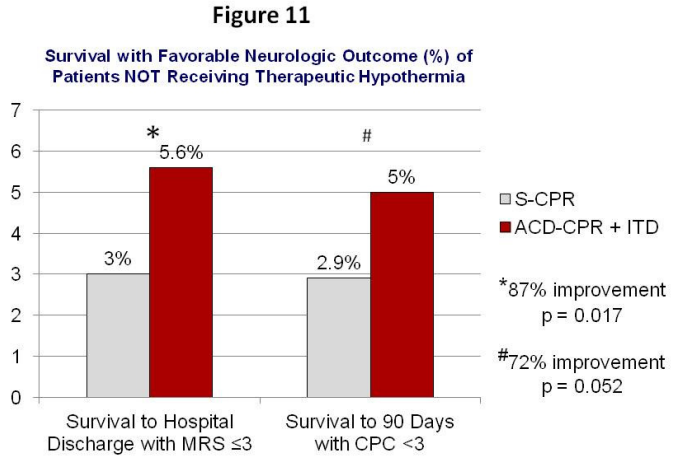


Figure 11. Neuro-Protective Benefits WITHOUT Hypothermia

For those patients who DID NOT receive therapeutic hypothermia, use of ACD-CPR plus an ITD was independently associated with a nearly two-fold increase in the number of survivors with favorable neurological function at the time of hospital discharge and 90 days after the cardiac arrest (NS).[9]



Other Key Findings:

- The overall rate of major adverse events, including chest fractures, was not significantly different between groups. There were more reports of pulmonary edema in the Intervention group, coexistent with increased survival in this group.
- Neurologic function was similar between groups at 90 days and one year after cardiac arrest. There was no increase in the number of patients with severe neurologic impairment in the intervention group.
- Results were consistent across study sites, patient age groups and gender.
- Time to device placement was critical and impacted survival. EMS personnel were able to place the study devices, on average, within approximately 30 seconds of initiating CPR. Subjects who received the device combination within five minutes realized a 68% survival benefit, whereas subjects who received the device combination within 6 – 10 minutes had a 44% survival benefit.

CONCLUSIONS

- Use of ACD-CPR plus an ITD was safe and effective.
- ACD-CPR with augmentation of negative intrathoracic pressure using an ITD improves long-term survival (to hospital discharge) with favorable neurologic function and the survival benefit persisted to one year following cardiac arrest.
- In patients with poor neurological function at hospital discharge, use of ACD-CPR with an ITD and therapeutic hypothermia resulted in a six-fold improvement in neurological function by 90 days, compared to S-CPR with therapeutic hypothermia.
- In patients with out of hospital cardiac arrest from a variety of non-traumatic etiologies, ACD-CPR with an ITD resulted in a 38.5% increase in survival to hospital discharge with favorable neurologic function (p=0.027), and a 35.4% increase in survival at one year with favorable neurologic function (NS), compared to patients receiving S-CPR.
- In the absence of treatment with therapeutic hypothermia after cardiac arrest, survival rates with favorable neurological function at hospital discharge, and 90 days after cardiac arrest, were nearly twice as high with ACD-CPR plus an ITD compared to S-CPR, indicating that the combination therapy is neuro-protective, independent of in-hospital therapeutic hypothermia.
- The device combination of ACD-CPR and an ITD is feasible to teach and implement in variety of EMS environments.

FUNDING SOURCE

Funding for the ResQTrial was provided, in part, by a grant from the National Institutes of Health (NIH) (R44-HL065851-03). Advanced Circulatory Systems Inc. (ACSI) obtained an investigational device exemption (IDE G050062) from the Food and Drug Administration and the study was conducted under the Federal guidelines for exception from informed consent (21 CFR 50.24). Additional monies were provided to local sites through a variety of other grants. The contents of this document are solely the responsibility of ACSI and do not necessarily represent the official views of the NIH National Heart, Lung and Blood Institute.

STUDY SPONSOR

ADVANCED CIRCULATORY SYSTEMS, INC.
1905 County Road C West; Roseville, Minnesota 55113 USA
www.advancedcirculatory.com

Chief Medical Officer/Principal Investigator: Keith Lurie, MD

If you have questions about the ResQTRIAL, please contact us at 651-403-5600.

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[a] Version used in ResQTRIAL

[b] The generally cleared indication for the ResQPOD that is available for sale in the United States (US) is for a temporary increase in blood circulation during emergency care, hospital, clinic and home use. The ResQPUMP ACD-CPR Device and the version of the ResQPOD ITD used in the ResQTRIAL are not yet approved for sale in the US. Research is ongoing in the US to evaluate the long-term benefit of the ResQPOD for indications related to patients suffering from cardiac arrest. The studies listed here are not intended to imply specific outcome-based claims not yet cleared by the US FDA.