U.S. Department of Health and Human Services
NIH News
National Institutes of Health

National Heart, Lung, and Blood Institute

http://www.nhlbi.nih.gov

For Immediate Release
November 6, 2009

Contact: **NHLBI Office of Communications**
(301) 496-4236
nhlbi_news@nhlbi.nih.gov

NHLBI Stops Enrollment in Study on Resuscitation Methods for Cardiac Arrest

Different CPR Durations Found Equally Successful; CPR Device Does Not Add Benefit

Enrollment has ended early in a large, multicenter clinical trial comparing two distinct resuscitation strategies delivered by emergency medical service (EMS) providers to increase blood flow during cardiac arrest. The study's independent monitoring board and the National Heart, Lung, and Blood Institute (NHLBI), the lead sponsor of the study, stopped enrollment based on preliminary data suggesting that neither strategy significantly improved survival. One strategy compared different durations of manual cardiopulmonary resuscitation (CPR) by EMS providers before they assessed whether defibrillation was needed, and the other strategy tested the potential benefits and risks of an investigational device to maintain pressure in the chest during CPR.

After reviewing data on approximately 11,500 study participants, the study's Data and Safety Monitoring Board (DSMB) recommended on Oct. 23 that the NHLBI stop enrollment because sufficient data had been gathered, and continuing recruitment was unlikely to change the overall outcomes of the study. The board had no concerns about the safety of any of the interventions tested, and NHLBI accepted the DSMB recommendations on the same day. Researchers will continue to monitor study participants who agree to follow-up visits for up to six months. They will analyze and publish the final data in the coming months. The NHLBI is part of the National Institutes of Health.

"Survival rates for patients who suffer cardiac arrest before reaching a medical facility are tragically low," said Susan Shurin, M.D., deputy director of the NHLBI, who oversees clinical trials supported by NHLBI and accepted the DSMB recommendation. "This study provides important evidence to help inform first responders and other health care providers on safe and effective life-saving treatment options. We will continue to search for new ways to save lives in the precious few moments after cardiac arrest – and evaluate the benefits and risks of commonly used practices."

The Resuscitation Outcomes Consortium (ROC), the largest clinical research network to study prehospital treatments for cardiac arrest in the United States and Canada, tested both resuscitation strategies as part of the **P**rehospital **R**esuscitation using an **IM**pedance valve and **E**arly versus **D**elayed (ROC PRIMED) clinical trial. An impedance valve, also called an impedance threshold device (ITD), is a small, hard plastic device about the size of a fist that is attached to the face mask or breathing tube during CPR administered by EMS providers. The device is designed to improve circulation by enhancing changes in pressures within the chest during CPR. Researchers found that ITD use did not significantly improve or worsen survival rates for cardiac arrest patients.

The early versus delayed strategy compared two currently used timing strategies of assessing the heart's rhythm in relation to when CPR is started by EMS providers. The heart rhythm assessment is done to determine whether defibrillation to restore the heart to its normal rhythm is needed. The study compared patient survival rates after EMS providers performed at least 30 seconds of CPR before assessing the need for defibrillation with delivering three minutes of CPR before the assessment. Based on current study data, both timing strategies were equally effective.

EMS providers assess approximately 350,000 people with cardiac arrest in the United States each year. Only 5 to 10 percent of people who have sudden cardiac arrest survive. When administered as soon as possible, CPR and, in some cases, rapid treatment with a defibrillator – a device that sends an electric shock to the heart to try to restore its normal rhythm – can be lifesaving. When delivered by EMS professionals, CPR is a combination of chest compressions, to keep oxygen-rich blood circulating until an effective heartbeat is restored, and rescue breathing. Lay bystanders are encouraged to immediately begin CPR using only chest compressions until professional help arrives, according to the American Heart Association.

ROC PRIMED was designed to test the two promising strategies to increase the chance of survival without functional impairments of patients who suffer cardiac arrest outside of a hospital setting. To test the ITD strategy, patients were randomly assigned to receive standard CPR from participating EMS providers either with an ITD or with a non-working replica (sham) of an ITD.

In animal studies and in small studies in humans, the ITD has been shown to markedly increase blood flow to the heart and to raise blood pressure. Human studies have also showed a tendency toward improved short-term outcomes without adverse effects. A modified version of the ITD is approved by the Food and Drug Administration (FDA) for use in conditions other than cardiac arrest.

However, a large human clinical trial was needed to show whether the device significantly improves survival with preserved neurologic function. Patients with preserved neurologic function are able to carry out activities of daily living. In contrast, patients who suffer neurological damage following cardiac arrest may no longer be able to care for themselves due to injury to parts of the brain.

The study's preliminary results indicate similar survival rates of patients with preserved neurologic function between both groups of patients, suggesting that standard CPR without an ITD is as effective as using an ITD.

“While the ITD is based on a sound physiologic principle, in this study it did not appear to improve survival rates for adults in cardiac arrest outside of the hospital,” said Tom Aufderheide, M.D., a professor of emergency medicine at the Medical College of Wisconsin in Milwaukee and a ROC principal investigator. “We will continue to seek out and thoroughly test new devices as well as alternative applications that hold promise for saving the lives of cardiac arrest patients.”

The other principal strategy studied in ROC PRIMED was the timing of assessing the heart’s rhythm to determine whether defibrillation is needed in relation to when CPR is started. For patients randomly assigned to the Analyze Early group, EMS providers were instructed to perform CPR until they were able to analyze the patient's heart rhythm (approximately 30 to 90 seconds). Patients in the Analyze Later group received CPR for at least three minutes before their heart rhythm was analyzed. When indicated, defibrillation was provided.

Some smaller studies have suggested that longer periods of CPR before defibrillation might increase survival, while other studies have suggested that more immediate defibrillation -- when the patient is treated within two minutes after the start of cardiac arrest -- might be better.

“The ROC PRIMED study answers a long-standing question in the EMS community over whether it is better to defibrillate earlier or later when trying to resuscitate a patient,” said Ian Stiell, M.D., professor and chair of the Department of Emergency Medicine at the University of Ottawa, senior scientist at the Ottawa Hospital Research Institute, and a principal investigator for the ROC PRIMED Analyze Early vs. Later protocol. “Both techniques appear to be equally beneficial."

Myron Weisfeldt, M.D., ROC Steering Committee chair and director of the Department of Medicine at the Johns Hopkins University School of Medicine in Baltimore, added, "Questions like this one – which address the relative benefits of current medical practices – are an important example of comparative effectiveness research and, in this case, can help advance emergency medical care.”

ROC PRIMED and other ROC clinical trials are conducted under strict U.S. FDA and Canadian guidelines that allow for patients in life-threatening situations to participate in research under an exception to explicit informed consent, according to U.S. and Canadian laws. This is necessary because, among other reasons, participants in cardiac arrest are unconscious and therefore cannot give consent. Before any patients were enrolled, communities were consulted about participation and made aware that informed consent will not be obtained for most study participants, as required by law.

To ensure patient safety during the study, the DSMB that monitors ROC studies reviews the accrued data approximately every six months or more frequently if needed. The ROC DSMB includes experts in trauma, cardiac arrest, statistics, ethics, and the conduct of clinical trials. During its interim data review on Oct. 23, the DSMB recommended stopping enrollment in both ROC PRIMED assessments based on results that suggest that both types of strategies were equally beneficial and that continued enrollment was unlikely to yield different results. The NHLBI accepted the recommendation, and ROC clinical sites stopped enrollment.

The ROC is a large clinical research network of 10 centers in the United States and Canada. Approximately 150 EMS and fire services organizations, involving more than 20,000 EMS providers who serve a combined population of more than 15 million people from diverse urban, suburban, and rural regions participated in ROC PRIMED. ROC research focuses on treatments for patients with life-threatening traumatic injury or cardiac arrest in real-world settings, typically where patients collapse or are critically injured, before they reach the hospital. Participating EMS providers receive intensive training, and give standard emergency care to all patients, with some patients randomly selected to receive the intervention to be tested in addition to usual care.

"The ROC is the largest research network to study real-world, pre-hospital interventions for cardiac arrest," noted George Sopko, M.D., ROC project officer in the NHLBI Division of Cardiovascular Sciences. "Conducting these studies through this robust and experienced network allows us to implement and compare clinical interventions in meaningful ways and to disseminate the results as quickly as possible so they can be applied to improve public health."

Earlier this year, the NHLBI stopped enrollment early for two ROC clinical trials that examined whether concentrated (hypertonic) saline improved survival over standard saline for trauma patients. Patients in the study were either suffering from shock due to significant blood loss or had experienced a traumatic brain injury. In both types of patients, hypertonic saline solution did not improve outcomes over the use of a standard saline solution.

The NHLBI is the lead federal sponsor of the ROC studies. Additional funding is provided by the NIH's National Institute of Neurological Disorders and Stroke, the Institute of Circulatory and Respiratory Health of the Canadian Institutes of Health Research, US Army Medical Research & Materiel Command, American Heart Association, Defence Research and Development Canada, and the Heart and Stroke Foundation of Canada.

Further information about this trial (NCT00394706) can be found at www.clinicaltrials.gov.

To interview an NHLBI spokesperson, contact the NHLBI Communications Office at 301-496-4236 or at nhlbi news@nhlbi.nih.gov. To interview Dr. Aufderheide, contact Toranj Marphetia at 414-456-4744 or toranj@mcw.edu. To interview Dr. Stiell, contact

Jennifer Paterson at 613-798-5555 x 73325 or jpaterson@ohri.ca. To interview Myron Weisfeldt, M.D., ROC Steering Committee chair, contact David March at 410-955-1534 or dmarch1@jhmi.edu.

More information:
- Resuscitation Outcomes Consortium: https://roc.uwctc.org/tiki/tiki-index.php
- Q&A on ROC PRIMED: http://public.nhlbi.nih.gov/newsroom/home/qanda.htm
- Sudden Cardiac Arrest:
http://www.nhlbi.nih.gov/health/dci/Diseases/scda/scda_whatis.html

Part of the National Institutes of Health, the National Heart, Lung, and Blood Institute (NHLBI) plans, conducts, and supports research related to the causes, prevention, diagnosis, and treatment of heart, blood vessel, lung, and blood diseases; and sleep disorders. The Institute also administers national health education campaigns on women and heart disease, healthy weight for children, and other topics. NHLBI press releases and other materials are available online at: www.nhlbi.nih.gov.

The National Institutes of Health (NIH) — *The Nation's Medical Research Agency* — includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. It is the primary federal agency for conducting and supporting basic, clinical and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit www.nih.gov.