Resource-Poor Resuscitation: Approach to Cardiac Arrest in a Developing Country

by

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ABSTRACT

RESOURCE-POOR RESUSCITATION: APPROACH TO CARDIAC ARREST IN A LESSER-DEVELOPED COUNTRY

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Background: As part of its Advanced Cardiac Life Support (ACLS) guidelines, the American Heart Association (AHA) recommends immediate cardiac monitoring for adults in cardiac arrest and, in cases of Ventricular Fibrillation (VF) or pulseless Ventricular Tachycardia (pVT), early administration of electric shocks with a cardiac defibrillator. In the United States, cardiac monitors and defibrillators are available in all hospitals for use during in-hospital cardiac arrest. Furthermore, the use Automated External Defibrillators (AEDs) is encouraged for out-of-hospital arrests. In geographically remote, resource-limited areas, cardiac defibrillators may not be readily available.

Objective: This paper aims to evaluate the availability and efficacy of in-hospital cardiac defibrillation and discuss the potential global health goal of improving defibrillator access in Peru.

Methods: An online literature search was performed looking for key words. Retrieved articles, their references, and past literature reviews on the subject were screened for relevance.

Results: In the United States, overall survival to discharge for cardiac arrest is low; however, there is well-established evidence that the use of ACLS guidelines improves outcomes for cardiac arrest. Patients who present in shockable rhythms are more likely to survive than those in non-shockable rhythms when a defibrillator is available. Identification of the precipitating acute medical illness is a moderate predictor of both initial rhythm and chance of survival. In Peru, etiologies of in-hospital cardiac arrest is somewhat different. Few scientific data are available for cardiac arrest outcomes or defibrillator availability in Peru.

Conclusion: Physicians practicing international medicine must recognize and adapt to differences in patient demographics and resource availability. In Peru and similar lesser-developed countries, basic public health need such as potable water and vaccines remain a priority. Efforts to improve outcomes for in-hospital arrest should focus on teaching high-quality CPR. When sufficient infrastructure is in place, improving access to defibrillators would be an appropriate next step.

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INTRODUCTION

My experience

My interest in a career in medicine has always gone hand-in-hand with an interest in global health. They were both ignited when I was seven years old and my father, a UT Southwestern graduate and family medicine physician, took me and the rest of my family to Kenya. For nine months, we lived and went to school in the missionary village of Tenwek while he worked as a volunteer doctor. He treated patients with malaria and HIV while we played in the paradise of this rainforest setting in the Kenyan highlands. On his days off, we took off in our four-wheel-drive truck and explored the rest of Kenya, from mountains to beaches to flamingo-filled volcanic lakes to, of course, safari plains. Since that time, my desire to become a doctor myself and treat patients in extremely resource-poor settings grew, eventually leading me to medical school at UT Southwestern and toward a career in emergency medicine.

As a student at UT Southwestern, I had several opportunities to learn global health alongside my traditional medical education. I spent two months in India during the summer between first and second year shadowing local physicians of various specialties. I also participated in the Global Health Interest Group, which brought in weekly speakers who shared their expertise and personal experiences working in medicine abroad. Finally, I worked up the nerve to apply for the program that had initially caused me to chose UT Southwestern as my first choice medical school: the International Medical Exchange Program.

The International Medical Exchange Program (IMEP) is a unique opportunity for medical students at UT Southwestern Medical Center to increase their knowledge of global health and medicine through immersion. For the past 8 years, a few students with a special interest in international medicine have taken time out of the traditional four-year career path to explore the world while learning medicine in widely different settings. At the end of their third year of medical school, these students pack up their belongings and travel together to Paris, France. They are enrolled as *externes* - medical students in their clinical years - at the University of Paris Descartes, where they complete two 3-month rotations in specialties at some of Paris' most prestigious hospitals. In the spring semester, they part ways and complete two more rotations in underdeveloped countries of their choice. This program takes a serious commitment of time and courage but provides an unparalleled opportunity to build a special knowledge in global health through complete immersion.

In Paris, I completed rotations in Dermatology and Emergency Medicine. For the spring semester, I rotated in Radiology in Buenos Aires, Argentina then traveled to Lima, Peru, for the last 3 months. I split my time in Peru between Infectious Disease (ID) and Orthopedic Surgery. During my six weeks on Infectious Disease, I was invited to travel to Iquitos, Peru and spend a week with some of the ID residents at the Hospital Iquitos. Iquitos is a port city on the banks of the Amazon river, inaccessible by car. It is the point of entry to *la selva* - the rainforest - for tourists and contains the nearest hospital for the indigenous peoples of the surrounding Amazon.

On the morning of my first day at Hospital Iquitos, I took a moto-rickshaw from my hostel to the hospital and was directed to the floor that housed the ID service. I shook hands with the residents and attendings then walked down the hall with them to start morning rounds. As we walked into the first hospital room, a large space with four hospital beds and open windows, we realized there was a single nurse performing CPR on a patient in one of the beds. I stepped aside and watched as the residents took over CPR and called for the crash cart. More nurses hurried in with the cart and the team alternated between administering CPR, breaths with a bag valve mask, and IV epinephrine. As I observed my first hospital code, I wondered what had happened to the patient and when they were going to bring in a cardiac defibrillator - the patients in this ward were not on monitors and the crash cart did not contain one. After about 25 minutes, they decided to terminate their efforts and declare the patient dead. We moved directly into rounds without taking time to discuss the case.

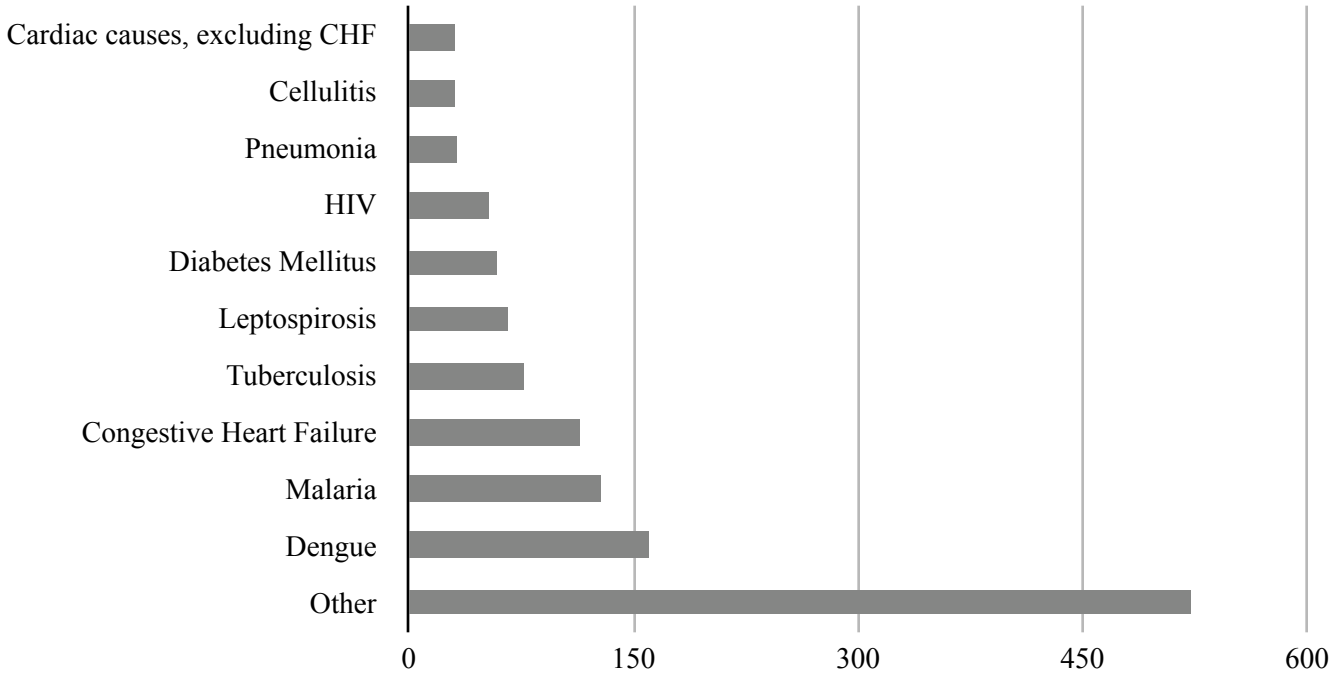
Between patients, I asked what he had died from and was told it was from sepsis. It dawned on me that, though these physicians and nurses were well trained in ACLS-type response to an in-hospital code, they did not have a cardiac monitor or defibrillator readily available on the ID floor. I realized my own ACLS training was designed for the resource-rich setting of a U.S. hospital and the typical U.S. patient population: more likely to arrest from a cardiac cause than other causes like sepsis. As a result of my experience in Iquitos, I decided to dedicate this thesis to further educating myself on the differences in the effectiveness of ACLS-type guidelines and the availability of defibrillation in resource-poor settings like Peru. I

will also explore whether, from a global health perspective, efforts to supply defibrillators and/or automated external defibrillators (AEDs) to providers in resource-poor settings can potentially improve patient outcomes.

A bit of context: Hospital Iquitos and the Peruvian healthcare system

The Hospital Iquitos is one of two hospitals in the city of Iquitos, "the capital of the Peruvian Amazon," in the Loreto region of northeastern Peru. With a population of 472,000, Iquitos is the largest city in the area and the sixth largest city in Peru. The Hospital Iquitos is a 120-bed hospital that has approximately 14,000 inpatient admissions and 73,000 emergency department (ED) visits per year. Dengue and malaria are the most common causes of death identified on the medical inpatient service (Table 1).[1] Cardiac defibrillators are available in the ED, OR and Intensive Care Unit (ICU).

Table 1: Causes of Death, Medical Inpatient Service, 2013[1]



The Hospital Iquitos is classified as a Category II - 2 by the *Modelo de Atención Integral de Salud (MAIS)* put forth by the Peruvian Ministry of Health (MINSA). In this model, a Category II - 2 hospital is a regional referral center providing comprehensive outpatient and inpatient care (Table 1). To qualify for this designation, the hospital must have an ED, inpatient services, ICU, operating and delivery rooms, pharmacy, blood bank and laboratory services. It must be staffed by specialists in Surgery, Pediatrics, Obstetrics, Internal Medicine, Cardiology, Neurology, Gastroenterology, Psychiatry, Ophthalmology, Orthopedic Surgery, Urology, Pathology, Radiology, and Otolaryngology.[2]

Table 2: Comparative Graph of the MINSA Categories for Healthcare Facilities[2]

Category	Description
I - 1	Health Services nurse's office
I - 2	Outpatient primary care physician's office
I - 3	Outpatient clinic, staffed by multiple physicians
I - 4	Outpatient hospital
II - 1	Local inpatient hospital
II - 2	Regional inpatient hospital
III - 1	Tertiary referral center
III - 2	Subspecialty center (e.g. cancer center, pediatric hospital)

The Peruvian healthcare system has been undergoing major reform for the past two decades as the government moves to expand insurance coverage and healthcare accessibility. The system is divided into two sectors, public and private. Almost 75% of citizens are covered through the public sector, which is further divided into two major entities. MINSA's *Seguro Integral de Salud* (SIS) is available to children and vulnerable adults including the poor, unemployed, and

part-time/informal workers; SIS covers about 50% of Peru's population. The other public insurance option is *Seguro Social de Salud* (*EsSalud*), which is provided to employees and funded by employer contributions. Despite these options, Peru still has disparities in health care access between urban and rural populations, the over-concentration of providers in urban centers, and a low national health expenditure (3% of GDP).[2,3,4]

According to the 2014 World Health Organization (WHO) estimates, Peru has a total population of 31 million and a gross national income (GNI) per capita of $6,360 USD. Seventy-nine percent of the population lives in an urban setting. The average life expectancy is 74.8 years. Only half of all deaths are properly registered, leading to poor data on mortality and an underestimation of cause-specific death rates. The leading reported cause of mortality is lower respiratory infections, which account for an estimated 75 deaths per 100,000 population. Ischemic heart disease is the second leading cause of death, causing 25 deaths per 100,000 population. Overall, communicable, maternal, perinatal and nutritional diseases cause 28% of deaths and noncommunicable diseases (i.e. cardiovascular disease, cancer, chronic respiratory diseases) account for 60% of deaths. For comparison, the United States has a GNI of $55,230 and a health expenditure of 8.3% of the GDP. Communicable, maternal, perinatal and nutritional diseases cause 6% of deaths and noncommunicable diseases account for 87% of U.S. deaths; ischemic heart disease is the leading cause of death (114 per 100,000 pop.) followed by dementia (98 per 100,000 pop.).[4]

Over the past 3 decades, Peru's epidemiological profile has shifted toward the typical pattern seen in industrialized nations. Prevention and treatment of communicable, maternal, perinatal and nutritional diseases has improved significantly since 1990, when these diseases caused 47% of deaths and

noncommunicable diseases caused only 45% of deaths.[5] However, there remains a large degree of disparity among the different regions of Peru. Rural inhabitants are 3 times more likely to be below the poverty line than urban inhabitants. *La selva*, the large climate zone of which Loreto is a part, only contains 14.3% of the total population. The indigenous tribes of the Peruvian Amazon have particularly poor access to healthcare and face the highest risk of vector-transmitted diseases, parasites and other transmissible diseases related to poor access to potable water and sanitation.[6]

OVERVIEW OF CARDIAC DEFIBRILLATION AND CPR

History

As exemplified by the famous fable of Benjamin Franklin and his kite, electricity was a popular area of experimentation for scientists in the late 1700s. As early as 1775, the Danish veterinarian P.C. Abdilgaard described killing chickens with an electric shock to the head, then subsequently reviving them with a shock to the chest.[7] In the 1770s, several publications described cases of human patients being resuscitated by electricity. Sixty years later, Jan Purkinje described the path of heart's electrical conduction through specialized fibers.[7] By the turn of the century, the electrocardiogram (ECG) had been invented and used to diagnose the different types of cardiac arrhythmias. In 1899, physiologists Jean Louis Prevost and Frederic Battelli performed the first true, internal defibrillation on a dog.[7] Experiments in defibrillation continued with increasing interest in the 1920s; the idea that chest compressions and rescue breaths could aid the flow of blood and air also stimulated interest in the scientific community. In 1956, Boston cardiologist Paul Zoll designed and successfully developed a human external defibrillator.[7] In 1960, Kouwenhoven et. al published an article in JAMA titled "Closed-Chest Cardiac Massage", the first study to demonstrate that external chest compressions improved circulation to a heart in ventricular fibrillation until defibrillation could be performed.[8] The defibrillator design was improved upon in the 1960s, finally culminating in the creation of a safe, portable trans-thoracic defibrillator. Its popularity and uses have continuously expanded, and today in the United States we have an expansive modern system for both in-hospital and out-of-hospital defibrillation.[7]

The rhythms of cardiac arrest and their causes

According to a standardized, internationally-accepted list of terms for use in resuscitation research known as the revised Utstein-style definitions,[9] cardiac arrest is "the cessation of cardiac mechanical activity as confirmed by the absence of signs of circulation.[9]" A resuscitation attempt is an attempt to restore life through emergency care techniques such as defibrillation, cardiopulmonary resuscitation (CPR), and breathing; CPR is "an attempt to restore spontaneous circulation by performing chest compressions.[9]" The end goal of a resuscitation attempt is the return of spontaneous circulation (ROSC), which is defined as "the restoration of a spontaneous perfusing rhythm that results in more than an occasional gasp, fleeting palpated pulse, or arterial waveform.[9]" "Survival" in the in-hospital setting means ROSC is sustained for more than 20 minutes. In the Ustein reporting style, cardiac arrest is "presumed to be of cardiac etiology unless it is known or likely to have been caused by" a non-cardiac cause.[9]

While cardiac arrest is an inevitable and defining moment in every death, there are four main cardiac rhythms associated with "the cessation of cardiac mechanical activity" that can be seen immediately following a loss of pulse. These rhythms include ventricular fibrillation (VF), pulseless ventricular tachycardia (pVT), asystole, and pulseless electrical activity (PEA). Of these four, only VT and pVF are "shockable rhythms" - treatable with cardiac defibrillation.[10]

A subset of cardiac arrest referred to as "sudden cardiac death (SCD)" is defined as "the unexpected natural death from a cardiac cause within a short time period, generally ≤1 hour from the onset of symptoms, in a person without any prior condition that would appear fatal.[11]" SCD is an area of special interest in the United States because it represents 20% of all mortality in industrialized countries

and, largely occurring without warning in a seemingly healthy population, has a devastating psycho-social impact on society. Because sudden cardiac death occurs unexpectedly, most cases occur outside of the hospital.[12] Though the epidemiology of SCD is incompletely understood, it is believed that the majority of sudden deaths are caused by ventricular tachyarrhythmias triggered by either acute coronary events (i.e. acute myocardial infarction or transient ischemia) or anatomic abnormalities (i.e. scarring) secondary to an old infarction.[13,14,15] SCD from VF/ pVT is the main target of U.S. efforts to make automated external defibrillators (AEDs) available in high-traffic areas. In contrast to patients with out-of-hospital arrests, most patients with in-hospital arrests are acutely ill.[17]

Primary ventricular fibrillation (VF) occurs without preceding hemodynamic deterioration, most commonly in the setting of severe ischemic heart disease such as a myocardial infarction.[13,18] VF can also occur secondary to circulatory shock or prolonged left ventricular (LV) failure, as is most common in hospitalized patients. [17] Other known causes of VF include digoxin or quinidine toxicity, hypothermia, blunt chest trauma, or severe electrolyte abnormalities.[19] Ventricular fibrillation is the initial rhythm in only 17% of in-hospital cardiac arrests.[17]

Ventricular tachycardia (VT) is the initial rhythm in 7% of in-hospital arrests.[17] Pulseless VT (pVT) is treated in the same manner as VF and has equivalent survival rates; thus, VF and pVT are grouped together in most resuscitation research publications and for the remainder of this paper.

Pulseless electrical activity (PEA) encompasses a variety of ECG patterns but by definition involves the presence of organized cardiac electrical activity in the absence of sufficient blood flow to produce a palpable pulse.[20] A significant minority of sudden deaths in the U.S. are caused by pulmonary embolism, which typically presents with an initial rhythm of PEA.[16] For in-hospital arrests, PEA is

the first documented rhythm in 30-37% of cases.[17,21,22] It is the initial rhythm in a significant proportion of deaths from primary cardiac causes (i.e. acute coronary occlusion). Prolonged, untreated or refractory VT and pVF can devolve into PEA. PEA also occurs secondary to defibrillation for prolonged VF/pVT, referred to as post-countershock PEA. Some sources differentiate between "true PEA" with a complete absence of cardiac mechanical activity and "pseudo-PEA" in which severe shock causes a profound decrease in blood pressure and pulselessness but myocardial movement is still detectable on echocardiography. True PEA, which includes secondary and post-countershock PEA, is thought to be a manifestation of left ventricular failure due to profound metabolic derangements seen in late-stage arrest and holds a dismal prognosis. Pseudo-PEA typically has a more normal ECG rhythm and has a markedly higher survival rate. Resuscitation research using Utstein reporting methods do not differentiate between true and pseudo-PEA. Treatment algorithms stress the importance of identifying and treating reversible causes of PEA, which account for a minority of PEA arrests.[24,25]

Asystole, also known as flatline, is a state of cardiac standstill with neither cardiac output nor ventricular electrical activity. It is the presenting rhythm in 35-40% of in-hospital arrests.[17,21,22] It is the final state of cardiac death; failed resuscitation attempts for VF, pVT, and PEA eventually devolve into asystole. As such, its etiologies encompass those of the above rhythms and survival rates are low.[22] Asystole and PEA are generally grouped together as "non-shockable rhythms" in treatment algorithms, which focus on reversible causes as stated above.

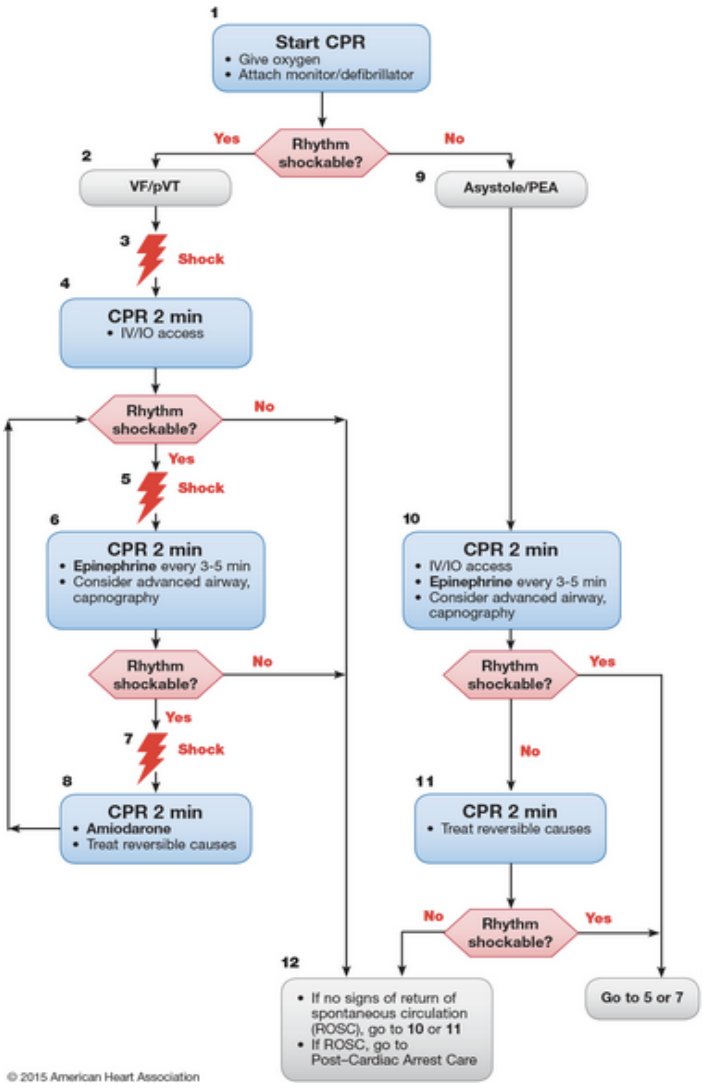
Science behind the shock

As its name implies, the cardiac defibrillator is utilized in an attempt to terminate abnormal electric cardiac conduction and "reset" the electrical conduction. The mechanism of defibrillation is incompletely understood, but its basic goal is to electrically interfere with the rapid, irregular reentrant circuits causing the tachyarrhythmia by applying a large enough stimulating field to activate all parts of the heart at once, including both refractory and recovered tissue.[26] If successful, normal electrical activity and subsequently normal cardiac motion will resume. Its use is indicated only for cardiac arrest with one of the two above rhythms identified; it is contraindicated for asystole, pulseless electrical activity (PEA), sinus rhythm, or a patient with a pulse. The defibrillator machine can also be used for synchronized cardioversion, which treats atrial fibrillation, atrial flutter, and supraventricular tachycardia by applying a low-energy shock when the cardiac rhythm is at the peak of the QRS complex. By timing the shock using a sensor, this avoids inappropriate application of the shock during repolarization, which can precipitate Ventricular Fibrillation.[10]

ACLS: THE AMERICAN APPROACH

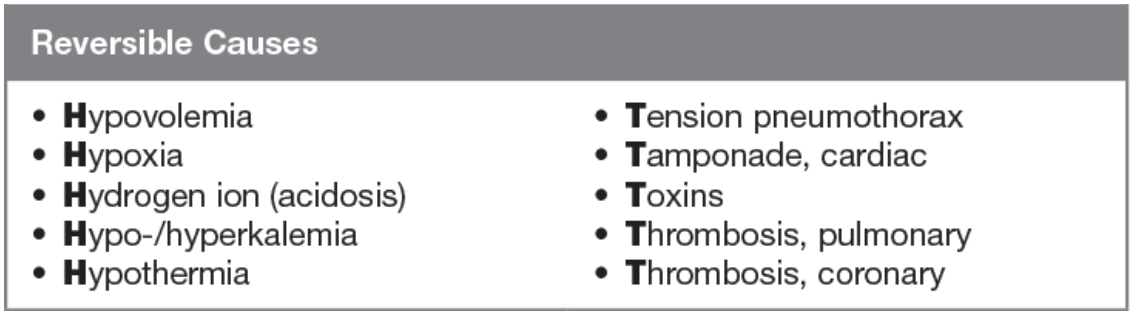
The Advanced Cardiac Life Support (ACLS) guidelines for the treatment of cardiac arrest were developed in 1979. The American Heart Association provides these guidelines in the form of a standardized training program for healthcare providers and responders. They also publish regular evidence-based updates to their national recommendations. "The foundation of successful ACLS is high-quality CPR, and, for VF/pVT, attempted defibrillation within minutes of collapse.[27]"

Figure 1. Adult Cardiac Arrest Algorithm - 2015 Update[27]



The three initial actions that are recommended in cases of adult cardiac arrest are: start chest compressions, give oxygen, and attach monitor/defibrillator to the patient (Figure 1). The next steps are to check the cardiac rhythm and, if VF or pVT is identified, administer a shock. If asystole or PEA is present, epinephrine is administered, reversible causes are treated, and CPR is continued for 2 minutes, at which time the monitor is rechecked for an organized or shockable rhythm.[27]

Figure 2. Reversible Causes of Cardiac Arrest[27]



With CPR and treatment of reversible causes, asystole and PEA can sometimes convert either to pulsatile rhythm (ROSC) or to VT/VF, which can then enter the "shockable rhythm" arm of the ACLS algorithm and be treated with defibrillation. To aid providers in remembering the potentially reversible causes of PEA, ACLS guidelines describe the "H's and T's" of cardiac arrest, as listed in Figure 2 above. For the three obstructive causes of PEA/asystole arrest - tension pneumothorax, cardiac tamponade, and massive pulmonary embolism - ACLS recommends the cause-specific treatments of needle thoracotomy, pericardiocentesis, and systemic fibrinolysis or embolectomy, respectively. Hypovolemia, including from massive blood loss, septic shock with hypovolemic

shock symptoms, and vasogenic shock from anaphylaxis, should be treated with aggressive volume resuscitation.[27]

Beyond those listed above, research has failed to show a benefit from most proposed cause-specific treatments.[24,25,27] Nevertheless, ACLS makes several treatment suggestions for the remaining "H's and T's" on the list above in addition to standard ACLS care. A few examples include calcium chloride to stabilize the cardiac myocyte in hyperkalemia, hydroxycobalamin and 100% oxygen to treat cyanide poisoning, naloxone for opioid overdose, antidigoxin Fab for digoxin poisoning, sodium bicarbonate for cyclic antidepressant overdose, and resuscitative thoracotomy for select trauma patients. Extracorporeal membrane oxygenation (ECMO) has been proposed for use in select cases as a means to buy time to treat suspected reversible causes.[27]

If ROSC is achieved, there are several ACLS recommendations that have been shown to improve survival. These include management of hypoxia and hypotension, coronary reperfusion for suspected myocardial infarct, and targeted temperature management to improve neurologic outcome for unconscious patients.[27]

Successes and shortcomings of the American model

The ACLS guidelines state that "for victims of witnessed VF arrest, early CPR and rapid defibrillation can significantly increase the chance of survival to discharge. In comparison, other ACLS therapies such as some medications and advanced airways, although associated with an increased rate of ROSC, have not been shown to increase the rate of survival to hospital discharge.[27]"

Many studies have examined the survival outcomes after resuscitation for cardiac arrest. Most notably, the AHA sponsors a multisite in-hospital resuscitation registry using the Utstein Template system called the Get With the Guidelines Resuscitation registry, the largest registry of its kind.[17,21,22] Overall survival after in-hospital cardiac arrest in the United States is low, with 54% achieving ROSC but only about 20% surviving to discharge and about 15% with good neurologic outcomes.[17,21,28] As acknowledged by the AHA, no specific drug has been shown to improve long-term outcomes when given during resuscitation despite decades of research.[29] In fact, several recent studies have shown that epinephrine administration is associated with lower rates of survival to discharge.[30,31] However, significant improvements in overall survival have been made due largely to improved quality of CPR and time to defibrillation, but also thanks to advances in post resuscitation care.[28,32] Studies have shown that close adherence to ACLS protocols leads to increased ROSC rates.[33,34]

As suggested above, initial monitored rhythm is a significant predictor of outcome. In a study of 51,919 patients by Meaney et. al,[17] survival to discharge with an initial rhythm of VF or pVT occurred in 37% and a favorable neurologic outcome in 31%. Survival rates were only 10-12% for PEA/asystole, and favorable neurologic outcomes occurred in only about 8% of each. Resuscitation of patients in non-shockable initial rhythms led to conversion of the rhythm to VT or VF in 27% with PEA and 25% with asystole; however, these patients tended to do much worse than those who do not convert to a shockable rhythm (7% vs. 13%).[17]

Similarly, the cause of the arrest can predict outcome.[17] Most patients with in-hospital arrests are acutely ill. In one study of 84,625 patients, about 15% of in-hospital arrest patients had pneumonia and about 18% had septicemia; about 34% were admitted for heart failure and/or MI.[28] Meaney et. al found that 19% had congestive heart failure, 20% acute MI, 42% respiratory insufficiency, 27% pneumonia and/or sepsis, and 32% renal insufficiency; the precipitating factor in the arrest was progressive respiratory failure in 37% and/or circulatory shock in 39%. Patients with acute MI, history or arrhythmia, or CHF were more likely to have an initial rhythm of VT/pVF. Those with respiratory insufficiency, pneumonia/septicemia, or hypotension were more likely to have asystole/PEA. However, all groups had significant numbers presenting in every rhythm.[17] Survival rates by acute preexisting condition were 24% for MI, 17% for heart failure, 12% for respiratory insufficiency, 11% for hypotension, 11% for pneumonia, 10% for trauma, 8% for metastatic cancer, and 7.6% for septicemia.[35]

The AHA's Basic Life Support (BLS) guidelines are designed primarily for use by non-medical personnel for out-of-hospital arrests and, like ACLS, stress the importance of quality CPR and early defibrillation.[36] Automated external defibrillators (AEDs) are designed for use by a layperson with only this basic level of training. A bystander can apply the pads to a person's chest and the machine will analyze the cardiac rhythm and determine whether the person needs defibrillation. The machine will give audio-guided directions to the user during the entire resuscitation process for whether chest compressions should be resumed, chest compressions should be stopped so the machine can analyze the cardiac rhythm, or

if the machine needs to be charged to deliver a shock. This option allows a non-medical bystander to quickly start resuscitation interventions before medical personnel arrive. AED availability in U.S. public places such as schools, airports and shopping centers has increased significantly in recent years. A large, randomized, prospective trial showed that a structured response system implementing AEDs in public places increases survival after out-of-hospital arrest.[37] Furthermore, economic models and observational studies in the U.S. have shown that AED programs in high-risk public locations are cost effective in terms of the estimated value of life-years saved.[38,39] The AHA advocates "placing AEDs in targeted public areas such as sports arenas, gated communities, office complexes, doctor's offices, shopping malls, etc.[40]"

The Rest of the Industrialized World

The International Liaison Committee on Resuscitation (ILCOR) was created in 1992 to unite the resuscitation groups worldwide and present unified resuscitation guidelines based on scientific evidence. Members include the AHA, European Resuscitation Council, Resuscitation Council of Asia, Inter American Heart Foundation, and similar organizations from Canada, Australia, New Zealand, and South Africa. The ILCOR's recommendations are nearly identical to the AHA guidelines described above.[18,34]

HOW DOES IT TRANSLATE? RESUSCITATION PRACTICES AND CONSIDERATIONS IN PERU

Peru is member of the Inter American Heart foundation and the ILCOR. In 1999, the *Consejo Peruano de Reanimation*, similar in purpose to the AHA, was created. Peruvian medical journals, *Consejo* bulletins and Ministry of Health publications disseminated Spanish versions of the 2010 and 2015 International Consensus on Cardiopulmonary Resuscitation put forth by the ILCOR.[36,41,42] The *Consejo* recommends that all health personnel should be trained in life support and that defibrillators be available in all health facilities and reachable within 3 minutes of the arrest.[43] BLS and ACLS courses are available in Peru through the *Consejo* and private training organizations; the *Consejo* also hosts seminars in Lima with topics such as the use of the Utstein template and the latest evidence-based advances in resuscitation. Despite this, one study at Hospital Dos de Mayo in Lima found that hospital nurses had only a moderate level of knowledge about chest compressions, ventilations and early defibrillation, scoring between 57% and 80% on test sections over these topics; this suggests an inadequate level of training in these hospital employees.[44]

There is no national registry for resuscitation in Peru and the Utstein reporting style is not in widespread use. Published data comparable to the U.S. research described above are extremely limited. However, a single-hospital study of Utstein data from 148 patients at Lima's Hospital de Emergencias José Casimiro Ulloa found that in-hospital cardiac arrest occurred at a rate of 2.54 per 1000 patients and had a survival rate of only 2%; VF/pVT occurred in 24%, asystole in 47%, and PEA in 28%. Septic shock was the most common diagnosis (43%)

followed by trauma (23%). With respect to the relatively high ratio of non-shockable rhythms and low overall survival rate, the authors postulate that "the deficient emergency system that we have in our environment and the consequent delay in CPR generates an over-diagnosis of asystole as the initial heart rhythm. This is due to the fact that, for many cases of VF, the true rhythm had converted to asystole by the time access to a monitor was available to determine the victim's heart rate.[45]"

In a 2008 report, the president of the *Consejo Peruano de Reanimación* acknowledged that Peruvian healthcare institutions had not been able to develop a comprehensive strategy to adequately address the problem of cardiac arrest, which would require a level of medical infrastructure and personnel training above the capacity of the country. However, he believes the creation of the *Consejo* was one of Peru's greatest achievements in the field of resuscitation. Its main goals are to publish up-to-date, evidence based guidelines, train and certify personnel in life support, and promote epidemiological research using the Utstein system.[46]

Peru has made progress in cardiac arrest treatment by participating in international evidence-based initiatives. A law was passed in May 2014 requiring all shopping malls in Peru to have at least one AED.[47] However, information on defibrillator availability is not available. Similarly, scientific studies relating to AED outcomes in Peru are extremely limited; an exhaustive online search produced only a single case report of automated external defibrillation being successfully used by paramedics in 2008.[48]

Resuscitation outcomes in other developing countries

Though data on outcomes for cardiac arrest in Peru are very limited, some research exists on such outcomes in other developing nations. Some countries with a similar GNI per capita and healthcare expenditure that have published data

related to resuscitation outcomes include Iran, Turkey, Thailand, and China.[49,50] In Thailand, a 639-patient study of Utstein data at 2300-bed university hospital found a survival to discharge rate of 6.9%. Initial ECG rhythms were VF/pVT in 12.4%, asystole in 42.6%, and PEA in 35.2%. The most common underlying causes of arrest were respiratory failure (24.7%) and septic shock (23.3%). The hospital uses BLS/ACLS guidelines and each crash cart has ACLS drugs and airway equipment, but defibrillators are not found on every cart; defibrillators are present in the ICU, CCU, and ER but are shared between two or more general wards. Only 25% of patients in shockable rhythms received defibrillation within 3 minutes.[51] In Turkey, a study at Istanbul University Hospital showed a ROSC rate of 49.3% and survival to discharge rate of 13.4%. Patients with ECG monitoring at the time of arrest had significantly higher ROSC rates (62.3% vs. 40.7%).[52] In a multi-center study of 10,198 in-hospital arrests in Beijing, China, Shao et. al[53] found that ROSC was achieved in 35.5%, 9.1% survived to discharge, and 6.4% had a good neurologic outcome. Outcomes were better in the ICU than other areas of the hospital. In Iran, a study of 206 patients had a survival to discharge rate of only 5.3%; time to defibrillation was a major predictor of survival but shocks were delayed by 10 minutes or more in 55% of cases.[54]

India, Pakistan, and Uganda are among the countries with significantly lower GNIs per capita than Peru.[49,50] A retrospective study at a private hospital in Pakistan found that PEA was the most common initial rhythm (50%), followed by asystole (30%) and VF/pVT (19%); survival rates were relatively high, with ROSC occurring in 72% and survival to discharge in 19%.[55] In Uganda, Ocen et. al[56] studied resuscitation among ICU, OR and ED patients; ROSC was achieved in 7.4% and only 1.6% were discharged alive. The hospital has no established in-hospital medical emergency response system; some providers have BLS/ACLS training but the facility is understaffed. The cardiac arrest was unwitnessed in 63%

of cases and CPR was performed for only half of the witnessed arrests. Interestingly, the main cause of arrest was trauma and most patients (66%) were under 45 years old. In India, a study of 105 ICU patients had only one survival to discharge.[57] A prospective Indian study found that formal certified BLS/ACLS training of hospital staff led to a definitive improvement in resuscitation outcomes (23% survival to discharge in pre-BLS/ACLS period vs. 69.1% in post-training period).[58]

AED vs. manual defibrillator for in-hospital arrest in Peru

A new AED costs 5,000-15,000 Soles in Peru, which is equivalent to $1,000-$3,500 USD. The cost for a new manual defibrillator is about $7,000-$14,000. Given this price difference, would in-hospital use of the cheaper AED machine be a cost-saving option for low-resource areas? In terms of efficacy, AEDs successfully terminate ventricular fibrillation on the first shock in 84% and within 3 shocks in 96% of patients.[59] They are much easier to use and much less dependent on provider skills, which may be especially important in places with fewer life-support trained personnel. AEDs are less likely to deliver inappropriate shocks than paramedics or resident physicians using a manual defibrillator.[59,60] Studies comparing manual versus semiautomatic modes found that AEDs deliver the first shock faster.[61] However, they require a pause in CPR for rhythm analysis that is not required in manual mode.[60,62] Pre- and post-defibrillation pauses are associated with lower rates of ROSC.[63,64] Most studies comparing AEDs to manual defibrillators for in-hospital cardiac arrest have shown no difference in survival to hospital discharge for patients with an initial shockable rhythm,[59,61,65] but a large study of 11,695 inpatients found that use of an AED was associated with a lower rate of survival to discharge for patients in a non-shockable rhythm using an AED;

this effect was significant enough that overall survival for all rhythms was worse in the AED arm.[65]

Several practical issues must also be considered when determining whether the cheaper AED is an acceptable alternative to a manual defibrillator for in-hospital cardiac arrest. A hospital can expect to see and treat cardiac arrest as a regular occurrence. However, AEDs are specifically designed to be portable and stored for long periods of time without use. They are generally powered by a replaceable, non-rechargeable battery; typical batteries have a shelf-life of 1-5 years but only last for 200-500 shocks or 4-17 hours of operating time. The pads are disposable and intended for one-time use.[66] By comparison, manual defibrillators for in-hospital use are rechargeable. They are available with either one-time-use self-adhesive pads or permanent hand-held paddles. They can be used for both defibrillation and synchronized cardioversion. Most modern defibrillators for hospital use are multifunctional, meaning they can be operated in both manual and semi-automatic (AED-like) modes.[44]

Opportunity cost: public health priorities in Peru

In a resource-poor setting, it is extremely important to consider comparative cost-effectiveness when making determinations about the virtue of a given public health endeavor. Careful selection of interventions with high cost effectiveness maximizes improvements in health in an environment of budget constraints. It is an error, and unfortunately a common one, for a low- to middle-income country to pursue sophisticated approaches to medical care that result in relatively low health gains per dollar invested. Instead, they should focus on finding the inexpensive interventions that yield dramatic improvements in morbidity and mortality. For instance, a million dollars spent on childhood vaccines saves an estimated 50,000-500,000 disability-adjusted life years (DALYs) whereas a million dollars

spent on cardiac bypass in high-risk cases saves fewer than 40 DALYs.[67] The world has seen some major successes in global health due in part to this approach, and we can learn from these successes; examples include polio vaccinations in Haiti, Peru's handwashing initiative, and Botswana's mass antiretroviral therapy program.[68] Peru's major public health needs parallel general priorities for developing countries; these include clean water and sanitation, vaccine-preventable diseases, zoonoses, HIV/AIDS, nutritional diseases, and maternal and reproductive health.[69] In Peru, 91% of urban populations and only 69% of rural populations have access to safe, potable water. Twenty percent of rural inhabitants have no access to sanitation facilities and practice open defecation.[70] The Loreto district faces particularly significant challenges in access to basic healthcare, high incidence of malaria, and access to sanitation and potable water.[69]

Interventions may be cost effective in high-income countries but not cost effective in low- or middle-income countries. In the case of defibrillators in Peru, the total cost per added unit is more than the price tag of the machine; both the cost and the added benefit are functions of the country's infrastructure and its health system's capacity.[67] Proper defibrillation relies upon personnel who are trained to perform CPR, operate the machine, and identify appropriate indications for use, although the training level is slightly lower if the machine has a semi-automatic setting. Only the minority of in-hospital arrest patients are found to be in shockable rhythms, and some of the survival benefit demonstrated in U.S. studies comes from post-arrest care such as coronary reperfusion and targeted temperature management; these may not be available in a resource-poor area. Furthermore, these hospitals may lack the necessary training and facilities to give basic ICU-level care to post-arrest patients. The machine also serves as a monitor and would allow the providers to identify PEA and asystole and move on to treatment of reversible causes, but this benefit likewise depends upon the availability of the

treatments for reversible causes, including trained physicians and equipment to perform needle thoracotomy, pericardiocentesis, embolectomy, etc.

DISCUSSION

Cardiac defibrillation and CPR were developed almost a century ago and remain to this day the two core treatments available for the treatment of cardiac arrest. In the United States, general recommendations for in-hospital cardiac resuscitation have been standardized for over 35 years. According to the American Heart Association's Advanced Cardiac Life Support protocol for adult in-hospital cardiac arrest, CPR and electronic cardiac monitoring should be initiated immediately and, if cardiac rhythm shows a "shockable rhythm" (ventricular fibrillation or pulseless tachycardia), defibrillation with an external cardiac defibrillator should be performed immediately. For "non-shockable rhythms" (asystole and PEA), ACLS espouses the use of epinephrine and cause-specific treatments. In the United States, approximately 20-25% of patients with in-hospital cardiac arrest initially have a shockable rhythm, and overall survival to discharge after in-hospital cardiac arrest is 17%.[17,28] The U.S. and other industrialized countries have adopted a similar set of resuscitation protocols and presented these guidelines as the standard of care for cardiac arrest internationally.

Given the relatively high survival rate of patients with in-hospital cardiac arrest in a shockable rhythm treated with defibrillation, there has been a national movement in the U.S. to increase awareness and availability of cardiac defibrillators. In addition to widely-taught treatment protocols that stress the importance of early defibrillation for in-hospital arrest, automated external defibrillators (AEDs) have been placed in high-traffic areas and successfully used for treatment of out-of-hospital arrest and AED use is a core component of basic life support training for non-medical professionals.[36,37]

Peru continues to make important economic and public health gains and its government is undertaking major efforts to achieve the same standards of

healthcare as in industrialized nations. It is still classified as a developing nation, however, and has a higher degree of economic disparity and fewer resources than in the United States. It is particularly deficient in rural areas and remote parts of the nation including the Loreto district. In these resource-poor settings, there are several key differences from in the U.S. that must be taken into consideration when discussing the treatment of in-hospital cardiac arrest.

First, defibrillators are less readily available in resource-limited or geographically remote areas. While the regional referral center Hospital Iquitos does have cardiac defibrillators, they are kept in high-acuity areas and are not part of every crash cart. Similarly, cardiac monitors that could be used to identify shockable rhythms in cardiac arrest are not present in some areas of the hospital, including the infectious disease ward. In order to follow the ACLS-type guidelines for adult cardiac arrest at Hospital Iquitos, it would be necessary for a defibrillator to be transported from other hospital areas when a code is called. This added time to defibrillation would significantly decrease survival of patients in an initial shockable rhythm.[71,72] Furthermore, smaller healthcare facilities in even more remote areas may have no defibrillator in the entire building. As an example, a small clinic in a rural village staffed by a single doctor or a few providers may be hundreds of miles from the nearest defibrillator.

Second, the etiologies of in-hospital cardiac arrest are different in developing nations. Particularly, primary heart diseases such as myocardial infarction cause a smaller proportion of deaths in Peru than in the U.S. and patients in Peru are more likely to die of infectious diseases than U.S. patients. Cardiac arrest from primary heart diseases are much more likely to have initial rhythms of ventricular tachycardia and ventricular fibrillation and thus benefit from defibrillation. On the other hand, sepsis and trauma are less likely to have a

shockable initial rhythm and thus benefit from defibrillators. In fact, cardiac arrest patients with these precipitating factors have a very poor chance of being successfully resuscitated irrespective of their presenting rhythm.

As a result of these major differences, it is necessary for physicians to consider the potential shortcomings of using ACLS-type in-hospital cardiac resuscitation protocols when practicing in resource-limited areas.

From a global health perspective, a cardiac defibrillator shortage represents a potential area for improvement through local, national, and/or international interventions. It is important to verify that a need for increased supply truly exists and that the intervention would improve health outcomes for the given population. Further, it is necessary to weigh the capacity for benefit against the cost of dedicating limited resources to the endeavor instead of to another.

CONCLUSION

Are ACLS-type protocols appropriate in Peru?

An important part of a doctor's vow to "do no harm" is avoiding futile treatments, even in end-of-life care. Futility is defined as "any effort to achieve a result that is possible, but that reasoning or experience suggests is highly improbable and thus cannot be systematically produced.[73]" It is the moral and professional obligation of the physician to decide whether a proposed treatment would be useful or futile based on "personal experience, experiences shared with colleagues, or consideration of published empiric data" before applying the treatment in the care of a patient.[73] A doctor practicing in an international setting has the additional responsibility to identify how resource limitations and epidemiological differences may alter their ability to make an accurate determination from the up-to-date evidence-based practices of their own country. Further complicating this task in the case of cardiac arrest is the fact that time is of the essence during the resuscitation period and this is not an ideal time or setting to make decisions about futility. The primary goal of this paper was to present both the evidence for protocols used by the U.S. and other industrialized countries and the crucial differences that exist in Peru with the hope that this information will aid doctors practicing in Peru to better make determinations of futility and treat cardiac arrest in a situation-appropriate manner. To some extent, the findings can reasonably be extrapolated, at the discretion of the physician, to other comparable health settings across the world.

In the United States, there is well-established evidence that cardiopulmonary resuscitation and, when indicated, the use of cardiac defibrillation improve survival

outcomes for in-hospital cardiac arrest.[28,74] We have therefore incorporated standardized guidelines recommending their routine use into training for medical personnel throughout the United States.[27] Protocols such as the AHA Adult Cardiac Arrest Algorithm help medical personnel work quickly and simultaneously in an emergency situation. Recent ACLS updates and U.S. advances such as extracorporeal membrane oxygenation (ECMO) can be seen as moving past the bread-and-butter resuscitation components of quality CPR and early defibrillation. However, the evidence used to form these guidelines came from studies conducted in the United States and similar industrialized settings with access to facilities and equipment meeting U.S. standards. Because defibrillation has been the standard of care for decades, there is no published data about survival rates for VF/pVT arrest when a defibrillator is not available.

The epidemiology of cardiac arrest in Peru is different than in the United States and American evidence does not perfectly translate to the Peruvian health setting. Though Peruvian data are limited, the overall survival rate for cardiac arrest is likely lower than in industrialized nations. Patients with non-shockable initial cardiac rhythms and/or certain precipitating factors such as trauma, sepsis and metastatic cancer have a very poor chance of surviving cardiac arrest to discharge. However, large U.S. studies have found that survival rates are still above zero for each of these groups. Thus, patients who arrest in the hospital have a chance of survival, though small, with immediate CPR even when a defibrillator is unavailable. Knowledge of the patient's acute comorbidities is not sufficient to make the difficult determination of prognosis in the pressured, hurried resuscitation setting. High-quality CPR is appropriate if there has been no pre-established "do not resuscitate" (DNR) order. If a defibrillator is available in another area of the hospital, providers should attempt to retrieve the machine as quickly as possible while providing high-quality CPR and treating suspected reversible causes. Above

all, the generally poor outcomes after in-hospital cardiac arrest should emphasize the importance of timely discussions of prognosis and the utility or futility of potential resuscitative treatments with patients and family members as soon as a risk of death is identified, regardless of the country in which one is practicing.

This paper does not discuss further ethical issues that often come into play when treating patients in foreign countries such as language barriers and local customs and attitudes about death. Doctors practicing international medicine should endeavor to understand these intricacies in addition to learning the epidemiological differences and resource availability in the local healthcare setting.

Improved defibrillator access in Peru: a worthwhile public health endeavor?

Despite the epidemiological differences between the U.S. and Peru, it is still true that some patients in VF/pVT would benefit from defibrillation and some patients in non-shockable rhythms would benefit from cardiac monitoring. The data above support the conclusion that lives would be saved by increasing defibrillator availability. However, the incremental cost effectiveness for this expensive and relatively rarely-used tool is far outweighed by that of other public health goals such as vaccinations and clean drinking water. In resource-poor parts of the world, endeavors to improve treatment of cardiac arrest should focus on teaching quality CPR. When sufficient infrastructure is in place, increasing availability of defibrillators would be the most appropriate next step; aside from CPR, defibrillators have much stronger evidence of benefit than other proposed resuscitative treatments. As a nation, Peru should increase overall funding for its healthcare system and continue its endeavors to improve healthcare access for rural populations, including the creation of a larger and more efficient system for the transferral of very sick rural patients to larger centers where they can receive adequate care.

Though AEDs are much cheaper and easier to use, manual cardiac defibrillators are the more appropriate tool for treating cardiac arrest in the in-hospital setting, though an AED is clearly better than nothing if the hospital cannot afford to purchase a manual defibrillator designed for in-hospital use. If hospital personnel lack adequate life-support training, a multifunctional defibrillator used preferentially in the semi-automatic setting would be ideal.

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VITAE

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