MEDICAL GRAND ROUNDS

ADVANCES IN

CARDIOPULMONARY RESUSCITATION

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When in the stream by accident, is found
A pallid body of the recent drown'd.
Tho ev'ry sign of life is wholly fled,
And all are ready to pronounce it dead,
With tender care the clay-cold body lay
In flannel warm, and to some house convey:
The nearest cot, whose doors still open lie
When mis'ry calls, will ev'ry want supply.

. . . But, ah! a fatal error oft has been,
When life, though latent, was not quickly seen.
Then thinking that the conclict all was o'er;
That life was fled, and could return no more,
Who much have wish'd, and yet despair'd to save,
Too rashly doom'd the body to the grave.
More patient thou, with ardour persevere
Four hours at least: the gen'rous heart will fear
To quit its charge, too soon, in dark despair;
Will ply each mean, and watch th' effect with care:
For should the smallest spark of life remain,
Life's genial heat may kindle bright again.

Rules of the Humane Society for Recovering Drowned Persons, 1767

Sudden death is a frequent occurrence in the United States. Trauma, suicide, and homicide make up a proportion of these incidents of sudden death. However, the greatest proportion of these sudden deaths are cardiac in nature. Cardiovascular disease has had a dramatic decrease in mortality over the last 30 years; but it still accounts for one-half of all mortality in the United States, or about 960,000 deaths per year. Of these deaths, about 525,000 are sudden in nature. However, only 2/3 of these sudden deaths are from coronary heart disease; the remaining 1/3 have other etiologies of heart disease. Of the 525,000 sudden cardiac deaths, 75 to 80% occur in patients with known cardiovascular disease. Thus, sudden cardiac death is the first symptom in 20 to 25% of patients.[1-5]

However, when the issue is approached from the starting point of a cardiac arrest, different statistics must be kept in mind. All patients who die have a cardiac arrest, as obviously it is the terminal event. There are almost 2 million deaths in the United States each year, of which 525,000 are sudden deaths in cardiac patients and only 350,000 sudden deaths in patients with coronary heart disease. Therefore, sudden cardiac death makes up about 1/4 of all cardiac arrests; and sudden cardiac death in patients with coronary heart disease make up between 1/6 and 1/5 of all cardiac arrests. This is important to keep in mind, as long-term survival is predominantly seen only in patients with sudden cardiac death from coronary heart disease.[1-11]

To understand the meaning of various reports on resuscitation survival, one must understand that the mix of patients is very different from one report to another making comparisons impossible. An EMS (Emergency Medical Services) system sees one subset of these patients. Table 1 shows what happens with 1000 patients who have a cardiac arrest in the pre-hospital setting. The numbers on this table represent the averages of several urban systems; in Dallas the rates are almost identical.

Table 1. Hospital Discharge Survival Rates from Pre-Hospital Cardiac Arrest
1000 Victims

	Long-term survivors
1000 victims with cardiac arrest	
400 victims non-cardiac etiology (survival 0.4%)	1
600 victims with cardiac arrest from heart disease	
270 victims with PEA(EMD) or asystole (survival 1.6%)	4
330 victims with cardiac arrest from heart disease and ventricular fibrillation	
132 victims that were not witnessed (survival < 1%)	1
198 victims with cardiac arrest from heart disease, VF, who were witnessed	
22 victims with long response time > 10 min (survival 0%)	0
176 victims with cardiac arrest, heart disease, VF, witnessed, good response	
76 victims survive long term	76
100 victims not resuscitated	
	Total 82

Table 1 does not tell the entire story. The 1000 victims at the top of the list were those on whom the EMS system began resuscitation. But how many victims did not have resuscitation started? Some patients already have rigor mortis, severe dependent lividity, decomposition, decapitation, or brain/cardiovascular injuries incompatible with life and no resuscitation is begun. In Dallas that percentage is 40%. Therefore, 667 victims did not have resuscitation attempted. The percentage where resuscitation is not attempted varies widely from one system to another. Obviously, this will influence the statistics. It also must be remembered that EMS systems do not handle all deaths. Victims with a

chronic illnesses often die in a hospital, a nursing home, a hospice program, or under the direct care of physician. In these circumstances, EMS may not be notified. As there is a large variation in such programs, different EMS systems may report varying numbers of chronically ill patients in their statistics. Another problem is that pure respiratory arrests are included in some series but not in others. Tables 2 and 3 summarize Table 1 in a different format.

Table 2. Long-Term Survivors of Out-of-Hospital Cardiac Arrest

Category of arrest	Number (%)
Cardiac patient with witnessed VF	76 (93%)
Cardiac patient with unwitnessed VF	1 (1%)
Cardiac patient with PEA or asystole	4 (5%)
Non-cardiac etiology	1 (1%)

Table 3. Long-Term Survival Rates from Out-of-Hospital Cardiac Arrest

	Rate, %
All arrests	8.2%
All cardiac patients	14%
All cardiac patients with VF	23%
All cardiac patients with witnessed VF	43%

When the same numbers are compared from one system to another, the results are very similar. However, an individual paper or report may not display the numbers in such a way as to make meaningful comparisons possible. Most papers in the literature report only cardiac patients. Many papers only report witnessed VF or all VF.

Return of spontaneous circulation (ROSC) occurs in about 10-30% of all arrests. Asystole and PEA also have a 20% ROSC; however, these patients usually die. Hence, ROSC or hospital admission looks very different from long-term survival.

In-hospital resuscitation also has a wide range of variables between hospitals. Hospitals have different mixes of patients. Some hospitals have large numbers of cardiac patients while others have larger numbers of cancer patients. Ages vary widely. An example is shown in Table 4 which compares hospitals that reported their results at the American Heart Association meeting in Atlanta.

Table 4. Survival to Hospital Discharge of In-Hospital Cardiac Arrest

	Hospital A	Hospital B
Cardiac arrest victims	270	339
DNR (Advanced directive)	190	31
Alive 24 hours after resuscitation	20	22
Awake at 24 hours after resuscitation	8	9
Awake patients made DNR after resuscitation	6	0
Discharged alive	2	7

It is obvious to see from this data that any comparison is difficult. As there were vastly different DNR rates, the selection of patients was very different. The fact that Hospital A made 6 of their awake patients DNR after the first resuscitation greatly changes the number of long-term survivors. Comparisons between hospitals are extremely difficult and usually meaningless unless detailed breakdowns of cases are used with similar reporting standards.

There are many other problems that must be recognized in order to evaluate many reports in the literature.

1. The only large subgroup of survivors is witnessed ventricular fibrillation in cardiac patients. Studies with 1000 victims do not have enough power to determine the benefits or lack of benefit in patients without cardiac disease, patients with unwitnessed arrests, or in patients with asystole or PEA (EMD).
2. Cardiac output during CPR does not always correlate to return of spontaneous circulation (ROSC). Many studies have shown increased flow but no difference in initial resuscitation rates or long-term survival. Some studies have shown increased cardiac output with a technique or drug, only to have a lower initial resuscitation rate and/or a lower long-term survival rate.
3. ROSC does not always correlate with long-term survival. Many techniques or drugs can initially obtain an increased initial resuscitation rate but make no difference in long-term survival.
4. Human studies have many variables that cannot be controlled. Techniques may vary between two groups, accounting for differences that are reported to be due to a drug.
5. Animal studies may not be predictive of long-term survival. Animal models can control a lot of variables and are a good method to evaluate mechanisms. However, animal models can only use ROSC as an endpoint and not long-term survival due to the fact that standards for humane treatment of animals require animals to be euthanized as soon as the protocol ends, prior to allowing the animal to awaken. Since ROSC does not necessarily correlate with long-term survival, animal data must be examined with certain skepticism.

Therefore, large, randomized trials are needed to try and gain insight into long-term survival. Large, randomized trials can also run into problems. Table 5 shows one preliminary report that I reviewed on a technique to improve survival. The study reported that the technique improved survival in cardiac patients from 14% to 20% and was significant at the $p=0.001$ level.

Table 5. Survival from Out-of-Hospital Cardiac Arrest with Two Different Techniques

	Technique A	Technique B
All systems	20%	14% p=0.001
System A	21%	19%
System B	20%	21%
System C	20%	4%

When the study was looked at in detail, the significant difference was not due to technique A being better than technique B, but was due to System C not properly using technique B. These problems make research and data collection in cardiac arrest extremely difficult and very hard to properly analyze. Hence the guidelines that have been developed are consensus guidelines by experts trying to extrapolate studies that leave much to be desired.[1]

ETIOLOGY AND RISK FACTORS

Whenever autopsy or resuscitated patient series are examined, about two-thirds of patients suffering a cardiac arrest have coronary artery disease. The distribution of the coronary artery disease is similar to that seen in patients with stable angina, acute myocardial infarction, or unstable angina. About 40-50% of patients with any of these presentations will have three vessel coronary artery disease, 30% have two vessel coronary artery disease, and 20 to 25% have one vessel coronary artery disease. Thus, the distribution of coronary artery disease is not different in patients who suffer cardiac disease. The majority of sudden deaths from coronary artery disease do not have myocardial infarction. It appears that the most frequent mechanism is coronary artery disease causing ischemia in the presence of ventricular ectopy; the ischemia alters fibrillation threshold, making the ventricular ectopy lethal. This mechanism may partially explain why control of ventricular ectopy does not reduce mortality; however, control of ischemia and platelet function will reduce mortality. The second most frequent mechanism is an acute myocardial infarction. The balance of sudden cardiac deaths are due to other forms of heart disease including cardiomyopathies (both hypertrophic and dilated), valvular heart disease, and hypertensive heart disease. Cardiac conduction abnormalities are associated with an increased incidence of sudden death, including the QT prolongation syndromes, the pre-excitation syndromes, and heart block. Many drugs can also cause sudden death by various mechanisms. Metabolic causes, including hypokalemia, hyperkalemia, and hypomagnesemia, also can play a role. In some cases no etiology can be found.[1-22]

Since the majority of sudden cardiac death victims have coronary artery disease, it is not surprising that the risk factors for coronary artery disease are the same risk factors as for sudden cardiac death. The major modifiable risk factors are smoking, hypercholesterolemia, hypertension, and lack of exercise. Diabetes mellitus is a major risk factor that can be treated. However, the impact of treatment of diabetes to modify cardiovascular risk is debatable. Equally important, but not modifiable, major risk factors include family history, increasing age, and the male sex. Stress and obesity are also risk factors, but they are not as important as those mentioned above. Besides atherosclerosis risk factors, there are some additional risk factors for sudden cardiac death: The presence of ventricular ectopy also correlates with sudden death. The more frequent and the more complex the ventricular ectopy, the greater the risk of sudden cardiac death. Poor ventricular function is also a predictor of sudden death. The worse the ventricular function, the greater is the risk of sudden cardiac death. Thus, many risk factors for sudden cardiac death can be recognized.[1]

MECHANISMS AND RATES OF SURVIVAL

In patients with cardiovascular disease, the dominant mechanisms of cardiac arrest is ventricular fibrillation or ventricular tachycardia. Though the exact incidence is not known, estimates have ranged from 60 to 90% incidence of ventricular fibrillation as the mechanism in patients with cardiovascular disease. Over the last two decades, the percentage of cardiac patients has been declining, the percentage of cardiac patients with ventricular fibrillation has been declining, and the average age has increased from 53-55 years to 65-71 years. In older patients more PEA or asystole has been observed. A second major mechanism is pulseless electrical activity (PEA) or electromechanical dissociation (EMD). PEA is a common mechanism in patients who have hypovolemia or hypoxia; thus, it is frequently seen in traumatic arrests. PEA can also be seen in cardiac patients with very severe cardiovascular disease. Asystole is usually a secondary arrhythmia. Primary asystole can occur particularly in patients with infra-His heart block (Mobitz II). However, the vast majority of patients with asystole probably had ventricular fibrillation or PEA first, then after 20 to 30 minutes or longer finally became asystolic.[1,6-10,14-17]

Survival from cardiac arrest is primarily from victims of ventricular fibrillation or ventricular tachycardia. Survivals of 30 to 40% have been achieved in the pre-hospital arena. Coronary care unit survivals of greater than 90% have been achieved when the cardiac arrest was not associated with preexistent shock. Survival from asystole and PEA has been very poor, less than 5%. In fact, 95 to 97% of the survivors at hospital discharge had ventricular fibrillation or ventricular tachycardia as the mechanism of arrest. Hence, ventricular fibrillation and ventricular tachycardia are the mechanisms of cardiac arrest that have the greatest chance of survival.[1,6-10,14-17]

TREATMENT

Resuscitation and the Chain of Survival

When the studies of successful resuscitation from cardiac arrest are examined, there are four dominant factors that differentiate survivors from non-survivors. These factors are time, defibrillation, drugs (particularly epinephrine), and CPR. Time to defibrillation is the most important determinant of survival. Time to epinephrine and time to CPR are also important determinants. CPR only widens the window of time for which defibrillation or epinephrine can be effective. Thus, CPR should be looked upon as a holding action, a losing holding action that merely prolongs the window of opportunity. Most of the long term survivors of cardiac arrest are victims who had a witnessed cardiac arrest from ventricular fibrillation or ventricular tachycardia, who had CPR begun within four minutes, and who had defibrillation and advanced cardiac life support within seven to eight minutes. The American Heart Association has identified the chain of survival with four steps -- early access, early CPR, early defibrillation, and early advanced cardiac life support.[1]

Early Access

Rapid recognition of the problem and activation of the emergency medical service (EMS) system is essential. Whenever unresponsiveness is recognized outside the hospital, EMS should be activated through the 9-1-1 system. Inside the hospital, the call for assistance should be made to the appropriate communication point for the hospital (code team, code blue, doctor heart, etc.). One problem outside the hospital is that 9-1-1 is not universal. It is present in many urban areas, but not in rural areas and smaller towns. Only four states have universal 9-1-1 today; only seven more states have laws establishing universal 9-1-1 by the year 2000. Hence, the physician must instruct patients on the proper method of interacting with the EMS system where the patient lives; the physician must recognize that this may be different from where the physician is located. Rapid recognition also is a problem. When a patient has a myocardial infarction, the patient frequently delays for more than two hours, but one-half of all deaths occur within the first hour of an acute myocardial infarction. To prevent sudden death, patient and family education is needed so that rapid recognition can occur, with rapid access to the EMS system. The physician must take time to adequately educate the patient and family concerning the proper times and mechanisms of system activation.

Early Cardiopulmonary Resuscitation (CPR) -- Basic Life Support (BLS)

Early initiation of CPR increases the victim's chance of survival by widening the window of opportunity for definitive therapy. CPR should be begun promptly and should continue until definitive therapy can be utilized. If a defibrillator is present and the patient is in ventricular fibrillation or ventricular tachycardia, immediate defibrillation should be accomplished; CPR should never delay defibrillation. Mass training of CPR had increased the number of rescuers performing CPR during the

1970's and early 1980's. However, the fear of AIDS and other communicable diseases has led to a decline in bystander or citizen CPR today. Recent studies have shown that bystanders performing CPR were related to the patient or were friends of the patient. It has become rare for a lay person to do CPR on a person they do not know. Hence, emphasis for training should be on family members and friends of patients who are at risk. CPR can be done by untrained callers with the aid of an EMS dispatcher. EMS dispatchers have been able to talk an untrained caller through the steps of CPR and have been successful at assisting in the resuscitation of victims. However, trained dispatchers who can give instructions are present in only a minority of EMS systems. The method of CPR (BLS) is outlined in Figure 1.[1]

Figure 1 TECHNIQUE OF CARDIOPULMONARY RESUSCITATION[1]

- **Establish unresponsiveness:** shake and shout
- **Rapid access:** call 9-1-1
- **Open the airway:** Tilt the head back using a chin or jaw lift
- **Establish apnea:** Place your ear over the patients mouth and nose, listen and feel for breath, watch for rise and fall of the chest
- **Ventilate:** Form a tight seal around the victim's mouth with a mask or your mouth (pinching off the nostrils if mouth-to-mouth) and deliver two breaths, allowing a brief time for exhalation
- **Establish pulselessness:** Feel for the carotid pulse
- **Begin chest compressions:** Place the heel of hands on the lower half of the sternum just cephalad of the sternal xiphoid junction and compress the sternum 1.5 to 2 inches at a rate of 80 to 100/minute
- **One rescuer CPR:** after 15 chest compressions, reopen airway and give two breaths - alternate at 15 compressions: 2 ventilations
- **Two rescuer CPR:** after five chest compressions, pause and allow second rescuer to give one ventilation - alternate at 5 compressions: 1 ventilation

One technique that has received a lot of notoriety is active compression-decompression (ACD) CPR, also know as plumber's helper CPR. Following a case report where a victim was successfully resuscitated using a plumber's helper, a number of reports have been generated using this technique. A commercial version has been developed with a suction cup that fits over the chest. The chest is compressed by pressing down on the chest. The device is then pulled up creating a negative pressure within the chest. This has been shown to provide adequate ventilation in animal models with an endotracheal tube in place without ventilations. This technique has also been shown to increase cerebral and myocardial blood flow as well cardiac output in both humans and animals. Several models have shown that this technique can increase coronary perfusion pressure. It has also been shown to increase ROSC (initial resuscitation). The technique does cause rapid rescuer fatigue due to the lifting. Two studies have tried to look at survival with this technique. Tucker reported that 64 arrests in 55 patients were randomized to ACD or standard CPR (this study had 270 arrests, 190 were excluded due to DNR status and 16 for other reasons).[27] The mean age of patients was 71 +/- 13 years with 23 men and 30 women.

Table 6. Randomized Trial of Active Compression-Decompression vs Standard CPR[27]

	ACD (%)	Standard (%)
Number of arrests	25	28
ROSC (initial resuscitation)	15 (60%)	9 (32%) $p<0.05$
24 hr survival	12 (48%)	6 (21%) $p<0.05$
Hospital Discharge	6 (24%)	3 (11%) NS
Duration of CPR	15 +/- 7 min	2.3 +/- 1.5 min $p<0.05$
Range of duration	(5-25 min)	(1-4 min)
Survivors/All		
Ventricular fibrillation	4/7 (57.1%)	3/8 (37.5%)
PEA	0/8 (0%)	0/9 (0%)
Asystole	2/10 (20%)	0/11 (0%)

A second trial by Cohen in 62 patients age 68 +/- 2 years with 45 men and 17 women has also been reported and are shown in Table 7.[28]

Table 7. Randomized Trial of Active Compression-Decompression vs Standard CPR[28]

	ACD (%)	Standard (%)
Number of patients	29	33
ROSC (initial resuscitation)	18 (62%)	10 (30%) $p<0.05$
24 hr survival	13 (45%)	3 (11%) $p<0.05$
Hospital Discharge	2 (7%)	0 (0%) NS
(6 awake pts made DNR after 24 hrs)		
Ventricular fibrillation	9	12
PEA	14	13
Asystole	6	8

It is obvious that the data is grossly insufficient to state that this technique has any benefit. It is certainly worth investigation but no wide-spread use.[23-31]

Vest CPR and alternating abdominal and chest compression have also been studied and increase cardiac flow and increase ROSC, but there is no evidence that they increase survival.[32-33]

Early Defibrillation

Early defibrillation is also an important link in the chain of survival. Defibrillators need to be quickly available wherever there is a risk of a cardiac arrest.[34-35] Every ambulance should have a defibrillator, but it is estimated that less than 25% of American ambulances have a defibrillator (a more realistic estimate is between 10 and 15%). Thus, there is a great need for defibrillators to be present on all ambulances. Automated defibrillators can be used by first responder units (fire engine, police cruiser, office building staff, stadium staff, etc.). Automated external defibrillators (AEDs) are attached to the patient with paste-on electrodes and use a built-in computer that recognizes first that there is good electrode contact, and then analyzes the rhythm for the presence of fibrillation waves and the absence of QRS complexes. It then charges the defibrillator and either discharges the defibrillator or advises the

rescuer to discharge the defibrillator. These devices are very rapid; some are totally automatic, in that they will shock the victim three times by simply pushing the "start" button once. Other devices require a two step interaction with the operator for each shock (one button activates the analysis, a second button delivers the shock). The Dallas Fire Department has studied the use of AEDs by trained individuals.[36] In Dallas beginning in 1985, we placed AEDs on 10 fire engines that were responding to districts that did not have an ambulance in the same district. Of 169 patients studied, 74 had ventricular fibrillation, 89 had asystole, and 42 had PEA. The device shocked 72 of 74 patients with ventricular fibrillation and none of the patients with asystole or PEA.

Table 8. Fire Engine Use of Automated External Defibrillators[36]

	AED	Control
Number of patients	169	200
Number of patients with VF	74	
Number shocked	72 (97%)	
Episodes of VF	115	
Episodes of VF shocked	104 (90%)	
Number admitted with perfusing rhythms	21 (12.4%)	10 (5%)
Long-term survivors	19 (11.2%)	6 (2.6%)

Kellermann[37] has done an almost identical study in Memphis and found no benefit. In Memphis, AEDs were placed on the 10 busiest fire engines. Those fire engines had ambulances in the same district. Usually the fire engine arrived simultaneous with the ambulance or the ambulance was first. In Dallas in the districts studied the fire engine was on the scene more than 2 minutes prior to ambulance arrival 62.7% of the time. A study of AEDs in Parkland Hospital on the cardiac stepdown unit revealed no improvement. The AED arrived simultaneously with the house staff and a manual defibrillator most of the time. AEDs may augment resuscitation rates in areas where there is a long arrival time for trained personnel with a manual defibrillator. But, an AED is no better than a regular defibrillator and does not improve survival unless it is there first and is used. Rapid defibrillation should be the goal for patients in ventricular fibrillation or pulseless ventricular tachycardia.

Early Advanced Cardiac Life Support

Before getting into algorithms or protocols for the management of cardiac arrest, drugs that are used in cardiac arrest will be reviewed with emphasis on some of the areas of debate.

Epinephrine - Epinephrine is the most important drug for use during a cardiac arrest. The mechanism of action of epinephrine is only partially understood. Epinephrine increases cerebral and cardiac blood flow during CPR, probably due to its alpha effects. It appears that the effects on cerebral and cardiac blood flow is more important than any of the beta effects of epinephrine. The minimum dose of intravenous epinephrine is 1 mg for average size adults or 0.01 mg/kg for children or very large adults. The upper limit of epinephrine dosage is not known. Higher doses of epinephrine have been suggested from both human and animal studies, because higher doses of epinephrine are associated with a higher return of spontaneous circulation (ROSC or pulse). Tables 9-11 show some of the results from studies of high dose epinephrine.[1,38-59]

Callaham[38] studied epinephrine 1 mg (SDE), epinephrine 15 mg (HDE), and norepinephrine 11 mg (NE) in 928 cardiac arrests. 762 were eligible to be enrolled in the study. 23% of the patients had ventricular fibrillation. The average age was 68 years; and the study had 69% men, with 58% of the arrests being witnessed. Bystander CPR was begun in 31% of the cases. 116 patients had ROSC, 104 patients were admitted to the hospital, and 48 patients were discharged alive. Table 9 reveals the comparisons.

Table 9. Comparison of High Dose Epinephrine, Standard Dose Epinephrine, and Norepinephrine in Pre-Hospital Arrests[38]

	HDE	NE	SDE	Significance
ROSC	20%	15%	11%	$p<0.02$
Inpatient ED	31%	27%	27%	
Hospital discharge	13%	17%	8%	
Survival of study patients given study drug	2%	2%	1%	

The problem with this study by Callaham is that of the 48 survivors, 35 had early defibrillation only. Only 13 surviving patients were given the study drug. Therefore, with three different rhythms and three groups means that the study drug only had one or two patients survive in a group.

Brown[39] also did a multicenter trial randomizing epinephrine 0.02 mg/kg (SDE) with epinephrine 0.2 mg/kg. This study had 1262 patients. The summary is shown in Table 10.

Table 10. Comparison of High Dose Epinephrine and Standard Dose Epinephrine in Pre-Hospital Arrests[39]

	HDE	SDE	Significance
ROSC	34.0%	29.9%	$p=0.13$
Admitted to hospital	22.0%	20.6%	
Discharged alive	4.6%	4.2%	

Stiell[40] had a similar result in 650 patients treated both in the pre-hospital environment and in the hospital.

Table 11. Comparison of High Dose Epinephrine and Standard Dose Epinephrine in Pre-Hospital Arrests[40]

	HDE	SDE	Significance
ROSC	17.7%	22.8%	
Discharged alive	3.2%	4.8%	

Thus, in randomized trials higher doses of epinephrine failed to increase survival at one hour, at hospital discharge, or to improve neurologic status even though there was an increased ROSC. Higher doses of epinephrine did not cause any increase in side effects. The problem with all of these studies is

that most of the survivors survived before the study drug was given and the numbers in any group are almost meaningless. It is possible that high dose epinephrine might be of benefit in PEA or in asystole; there are insufficient numbers to draw any conclusion other than to state that no improvement in survival has been seen with very small numbers. Therefore, higher doses of epinephrine may be used. Alternative regimens include high dose epinephrine 0.1 mg per kg every three to five minutes, intermediate dose epinephrine 2 to 5 mg every three to five minutes, escalating dose epinephrine 1 mg followed by 3 mg followed by 5 mg three minutes apart. If there is no intravenous access, epinephrine 0.1 mg per kg of 1:1,000 can be given down the endotracheal tube.[1,38-59]

Sodium bicarbonate - The use of sodium bicarbonate has been controversial. Evidence as to the benefit of bicarbonate has been contradictory. Sodium bicarbonate has been shown to be definitely effective and helpful in cases with known preexistent hyperkalemia. On the other end of the spectrum, sodium bicarbonate has been shown to be of no benefit and possibly harmful in cases of hypoxic lactic acidosis. In between are several situations in which bicarbonate might be helpful. It is probably helpful in cases of known preexisting bicarbonate-responsive acidosis, overdose of tricyclic antidepressants, and to alkalinize the urine in other types of drug overdoses. Sodium bicarbonate may be helpful in patients with prolonged arrests, in an intubated patient, or upon return of a pulse after a prolonged arrest; however, the evidence for benefit is only possible and not proven. If a decision to give sodium bicarbonate is made, the recommended dose is 1 mEq per kg.[1,60-82]

Magnesium - The use of magnesium has been controversial. Hypomagnesemia has been associated with increased ventricular ectopy and persistent ventricular fibrillation.[83] Tsuji[84] reporting from the Framingham study has shown correlations between PVCs and hypokalemia and hypomagnesemia. Table 12 shows the age adjusted prevalence of complex or frequent ventricular ectopy in relationship to potassium and magnesium serum levels.

Table 12. Age Adjusted Incidence of Complex or Frequent Ventricular Arrhythmias According to Serum Potassium or Magnesium Levels[84]

Potassium		Magnesium	
Serum K	% PVCs	Serum Mg	% PVCs
<4.4	7.9%	<1.77	6.7%
4.4-4.6	5.7%	1.77-1.87	6.1%
4.7-4.9	5.4%	1.88-1.97	6.1%
>4.9	5.1%	>1.97	5.2%

The odds ratio, when corrected for risk factors and left ventricular mass, was highly significant for ventricular ectopy to be linked with hypokalemia and hypomagnesemia independent of other factors.[84] It has also been suggested in several studies that patients with acute myocardial infarction will have less arrhythmias if given prophylactic infusions of magnesium. Seven trials were analyzed by metaanalysis and shown to have less arrhythmias when treated with magnesium. Table 13 reveals the combined data for these trials.[83]

Table 13. Mortality in Acute Myocardial Infarction Patients Randomized to IV Magnesium or Placebo[83]

	Magnesium	Control	Significance
Six trials	38/637 (6%)	69/629 (11%)	$p<0.05$
LIMIT-2	90/1159 (7.8%)	118/1157 (10.2%)	$p<0.05$

However, ISIS-4 reported a randomized trial of magnesium in 58,000 patients treated within 24 hours with IV magnesium for 24 hours or placebo. Table 14 reveals the magnesium data from ISIS-4.[85]

Table 14. Randomized Trial of IV Magnesium in Acute Myocardial Infarction[85]

	Magnesium	Control	Significance
Patients treated	27,413	27,411	
Cardiogenic shock	4.5%	4.0%	$p<0.05$
Heart failure	17.9%	16.6%	$p<0.05$
Cardiac arrest	3.9%	3.7%	NS
Stroke	1.0%	0.9%	NS
2° or 3° AV block	3.7%	3.5%	NS
Mortality (6 week)	1,997	1,897	
Mortality (6 week %)	7.28%	6.92%	$p=0.1$

North[93] reported a randomized double-blinded comparison of IV magnesium versus normal saline in patients with stable monomorphic ventricular tachycardia.

Table 15. Randomized Trial of Magnesium in Monomorphic Ventricular Tachycardia[93]

	Magnesium	Saline	Significance
Conversion of VT	6/20	3/23	NS
Reinducibility	15/20	17/23	NS
Cycle length of VT	315 msec	309 msec	NS

Thus, magnesium sulfate does not appear to be effective in monomorphic sustained ventricular tachycardia.

Therefore, there is no evidence of benefit with the routine administration of magnesium in patients with an acute myocardial infarction. The only patients who might benefit are those that are hypomagnesemic or have torsade de pointes.[1,83-87,93]

Antiarrhythmic Agents - The use of antiarrhythmic agents has not been definitively shown to be of benefit. The evidence supporting their use has been from small studies and comparative studies showing that one drug was as good as another. One interesting study was by Sanz[88] who compared prophylactic administration of lidocaine to prophylactic administration of magnesium in patients with acute myocardial infarction.

Table 16. Randomized Trial of Prophylactic Lidocaine vs Magnesium[88]

	Magnesium	Lidocaine	Significance
Mortality	1.5%	1.5%	NS
Major events	5.0%	26.0%	p=0.003
All events	11.0%	36.0%	p=0.003
Fever	31.0%	3.0%	p=0.001

As prophylactic magnesium was not of benefit, it appears that prophylactic lidocaine is worse than magnesium. Thus, antiarrhythmic therapy is recommended only in life threatening arrhythmias.

Aminophylline - A recent report revealed that 11 of 15 patients with asystole or bradycardic PEA who had failed epinephrine and atropine, responded to the rapid infusion of 250 mg IV of aminophylline. Only one patient survived to discharge.[89] As aminophylline can antagonize adenosine, more work is needed to see if this is of benefit.

Angiotensin II - An animal study has suggested that angiotensin II can improve coronary perfusion pressure and aid in resuscitation. Vasopressors of many types have previously shown to increase ROSC in animal models. Thus, this result is expected and is not of the level to warrant the amount of press that it has received.[90]

ALGORITHMS

Protocols for the major actions to be taken during a cardiac arrest by mechanism are shown in Figures 2, 3, and 4. These protocols are adapted from the 1992 guidelines published by the American Heart Association in the Journal of the American Medical Association.[1] Drugs should be given intravenously, if possible, during a cardiac arrest. It is preferable to give drugs in the upper extremity or in a central line. Drugs given in a leg vein or the femoral vein may take many minutes to get to the central circulation, as flow below the diaphragm during CPR is minimal. The flow during closed chest CPR is predominantly to the head and upper extremity. The recommended IV fluid is a non-glucose containing solution as higher blood sugars post-resuscitation correlates with worse outcome.[1]

Ventricular fibrillation (VF) and pulseless ventricular tachycardia

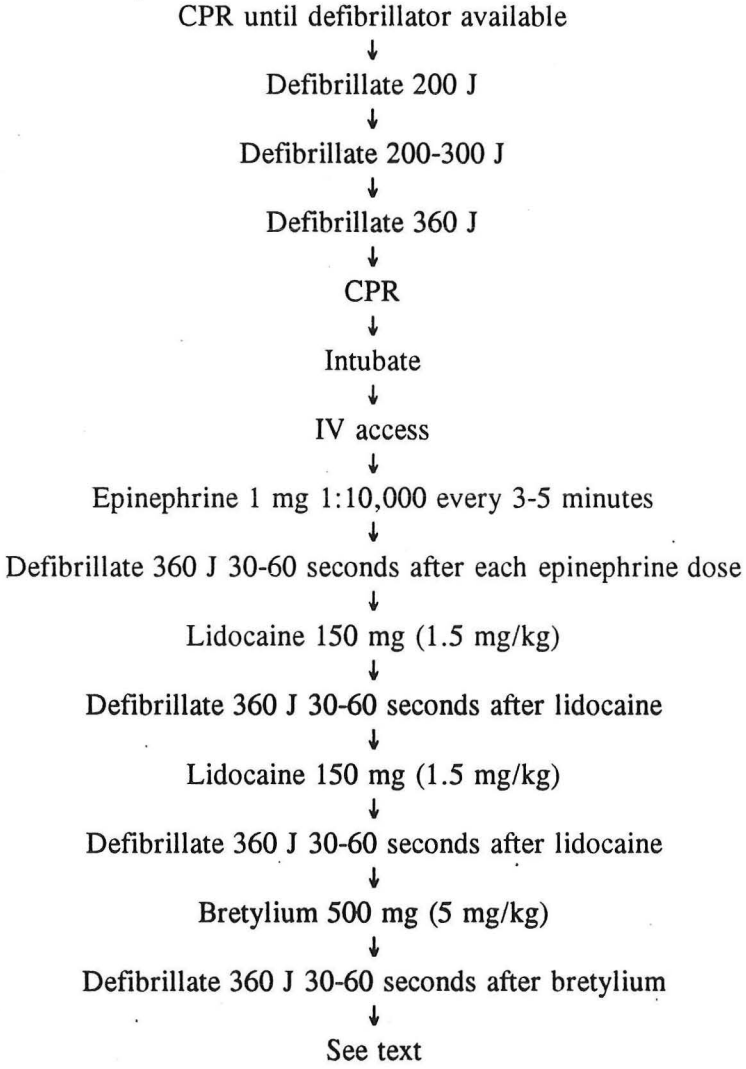
The patient should be defibrillated as rapidly as possible, as shown in the algorithm in Figure 2. When a manual defibrillator is used, check the rhythm after each defibrillation and after each drug. Check pulse after first three shocks, then after each subsequent shock and drug dose. When an automated defibrillator is used, do NOT check a pulse after each shock; only check after a group of three shocks. At any time the rhythm changes or a pulse is present, change to the appropriate protocol.

Antiarrhythmic agents that can be used during the VF protocol include lidocaine, bretylium, and procainamide. There is no clear cut advantage of any one of the drugs over the other. If lidocaine is used, it is recommended initially to give 150 mg or 1.5 mg per kg intravenously; repeat doses of 0.5 to 1.5 mg per kg (up to a maximum of 3 mg per kg) can be given. Bretylium 5 mg per kg intravenously can also be used followed by repeat doses of 10 mg per kg every five minutes; no maximum dose is known though most stop at 25-30 mg per kg total dose. Procainamide 30 mg per minute up to 1000 mg intravenously has also been used and is acceptable. The most common preference is to try lidocaine first

(as it is the least toxic), and then go to bretylium, if the lidocaine is not effective. Remember to always shock the patient 30-60 seconds after each dose of medication.

If the patient is refractory, then higher doses of epinephrine may be considered (see "Epinephrine" above). Sodium bicarbonate may be of benefit in a few patients (see "Sodium bicarbonate" above). Magnesium sulfate may also be of benefit in patients with torsade de pointes, suspected hypomagnesemic state, or refractory ventricular fibrillation. The recommended dose of magnesium sulfate is 1 to 2 grams intravenously over one to two minutes (see "Magnesium" above).

Figure 2 VENTRICULAR FIBRILLATION/PULSELESS VENTRICULAR TACHYCARDIA



Pulseless electrical activity (PEA)

The presence of organized electrical activity on the monitor with no palpable pulse is called pulseless electrical activity (PEA). This includes any rhythm without a palpable pulse -- electromechanical dissociation (EMD), pseudo-EMD, idioventricular rhythms, ventricular escape rhythms, bradyasystolic rhythms, and post-defibrillation idioventricular rhythms. The treatment algorithm is shown in Figure 3. In addition to the treatment shown in the algorithm, one must look for the cause and try to correct the cause. Table 17 shows possible causes of PEA with possible treatment. If one of these conditions is present, attempt to correct the cause. If the arrest is refractory, then higher doses of epinephrine may be considered (see "Epinephrine" above). Sodium bicarbonate may be of benefit in a few patients (see "Sodium bicarbonate" above).

Figure 3 PULSELESS ELECTRICAL ACTIVITY (PEA)

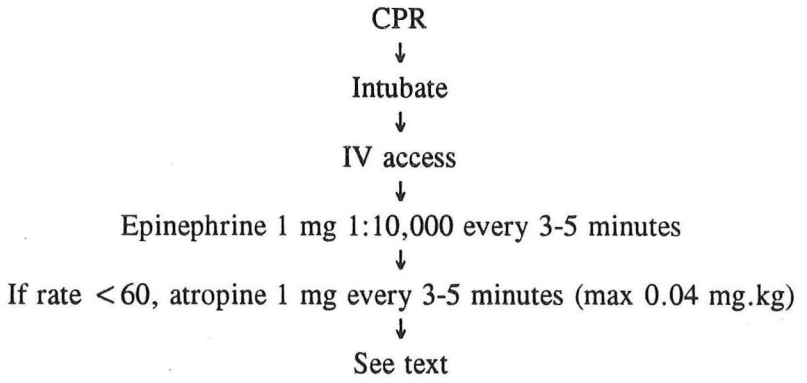


Table 17. CAUSES AND TREATMENT OF PULSELESS ELECTRICAL ACTIVITY

Possible cause	Possible therapy
Hypovolemia	Volume infusion
Hypoxia	Ventilation, supplemental oxygen
Cardiac tamponade	Pericardiocentesis
Tension pneumothorax	Needle decompression
Hypothermia	Rewarm
Massive pulmonary embolus	Surgery, thrombolytics
Hyperkalemia	Bicarbonate, calcium, dextrose
Acidosis	Bicarbonate
Drug overdoses	Specific antagonist
Massive myocardial infarction	Thrombolytics, angioplasty, surgery

Asystole

Asystole should be confirmed in two leads that are about 90 degrees apart (II and aVL) to make certain that the patient does not have ventricular fibrillation. If the patient has asystole, consider some of the causes that can be potentially treated -- these include hypoxia, hyperkalemia, hypokalemia, preexisting acidosis, drug overdose, and hypothermia. If the arrest is refractory, then higher doses of

epinephrine may be considered (see "Epinephrine" above). Sodium bicarbonate may be of benefit in a few patients (see "Sodium bicarbonate" above). There is no definitive evidence that pacing is of advantage in asystole; most authorities believe that if pacing is used it must be used early.[1]

Figure 4 ASYSTOLE

CPR
↓
Intubate
↓
IV access
↓
Transcutaneous pacing if available
↓
Epinephrine 1 mg 1:10,000 every 3-5 minutes
↓
Atropine 1 mg every 3-5 minutes (max 0.04 mg.kg)
↓
See text

Beginning and Terminating Resuscitation

The decision to begin CPR and resuscitation is based upon both medical and legal grounds. Resuscitation should be utilized in cases of sudden unexpected death that does not have a medical or legal contraindication for resuscitation. Medical contraindications to resuscitation includes rigor mortis, decapitation, decomposition, and severe dependent lividity. Traumatic injuries, with visually recognizable injuries to the brain or cardiovascular system that are not compatible with life, are also used by some authorities. Legal contraindications include court orders, advance directives to physicians, and in some states living wills. Resuscitation should not be begun when there is no chance of reversing the primary illness. Patients with terminal illnesses that can not be treated are not candidates for resuscitation in most circumstances. Terminal diseases might include certain end-stage cancers, end-stage AIDS, and cardiogenic shock that is refractory to therapy. With terminal diseases, the physician should discuss the situation with the patient and family and develop a mutually acceptable plan of action should a cardiac arrest occur.

Termination of resuscitation should be done in two different situations. If resuscitation is begun and then it is found that there was a reason not to begin resuscitation, it is reasonable to terminate resuscitation. Otherwise, resuscitation should be continued until it is obvious that the cardiovascular system is non-responsive. Most successful resuscitation victims are resuscitated in the first ten minutes of advanced cardiac life support. A few more are resuscitated when a reversible cause is found and treated. Hence, a rule of thumb is to discontinue resuscitation after 20 to 25 minutes of advanced cardiac life support when any treatable cause has been treated. Rarely, a patient can be resuscitated after prolonged efforts; however, neurologic impairment is frequent with prolonged effort. One exception to these times is hypothermia where a prolonged arrest can be reversed after partial rewarming.

EFFECTIVENESS OF RESUSCITATION

Most of the survival data that is in the literature is in white males. The results in women and other ethnic groups is not as clear. A recent study from Seattle has suggested that blacks have a worse outcome as compared to whites. The age adjusted incidence of out-of-hospital arrest was significantly higher in blacks than in whites; however,resuscitation was far lower in blacks as compared to whites (Table 18).[91]

Table 18. Comparison of Resuscitation Rates by Ethnic Groups[91]

	Blacks	Whites	
Age adjusted incidence of out-of-hospital cardiac arrests/1000	3.4	1.6	$p<0.05$
ROSC (Initial resuscitation)	17.1%	40.7%	$p<0.05$
Hospital discharge	9.4%	17.1%	$p<0.05$

The reason for this ethnic difference is not known. The authors have suggested delays in instituting therapy, less bystander-initiated CPR, poorer levels of health, or differences in the underlying cardiac disorders may have contributed to the differences. Men are more often resuscitated than women as more men have witnessed ventricular fibrillation in the younger years.

Cummins[92] has reported the 10 year survival of victims of cardiac arrest who were discharged alive after the initial arrest. Using life-table methods, men had a better 10 year survival after cardiac arrest than women. Younger individuals also had a better survival than older individuals.

Table 19. 10 Year Survival after Out-of-Hospital Resuscitation

Sex	% Survival	Age	% Survival
Men	40%	<64 years	48%
Women	28%	>64 years	25%

The gender difference was entirely due to age differences as the initial age for men was 63 and the initial age for women was 68 years. By using age-adjusted statistics, there was no difference in long term survival between men and women.

Thus, there appears to be good, long-term survival after resuscitation if the victim lives to hospital discharge. It should be noted that the 10 year follow-up was begun prior to implantable defibrillators that may well alter 10 year survival. It is easy to be pessimistic about the low rates of initial survival. However, when you compare survival versus the number of people treated, resuscitation has a very favorable outcome. Table 20 shows the relative save rates for several common cardiac therapies.

Table 20. Lives Saved per 1000 Treated with an Intervention

Intervention	Rate
Resuscitation	82/1000
Aspirin	20-30/1000
Thrombolytics	30/1000
ACE inhibitors	7/1000

SUMMARY

Resuscitation has improved slowly over the last 20 years. The important items that predict successful outcome are time, defibrillation, CPR, and epinephrine. There is need for more research to improve the initial success rate as well as the long-term survival.

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