Sudden Cardiac Death:
A Changing Syndrome

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"Tis a vile thing to die, my gracious lord,
When men are unprepared, and look not of it."
Shakespeare: *Richard III*
scene iii, act II, 1592

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Research interests: Sudden cardiac death
Paramedic programs
Early defibrillation programs

Historical Introduction

Sudden death is an entity which has provoked thought and interest for most of the recorded history of man. This interest has influenced literature, the stage, movies, and television which have used sudden death as an integral part of their dramas. Our running of marathon races is based upon the story of a warrior who ran home to Athens after the battle of Marathon in 490 BC to announce that the Athenians had defeated the Persians and dropped dead at the end of his report.[1] Sudden death has also spurred scientific interest for centuries. The Egyptians were interested in sudden death more than 4,000 years ago and associated sudden death with a description of coronary ischemia — "If thou examinest a man for illness in his cardia and he has pain in his left arm and breast and in one side of his cardia.....it is death threatening him."[2-3] From China, Pien Chio wrote in 500 BC that when every other pulse was felt, death would occur within days.[2,4] Hippocrates has several quotes relating to sudden death and coronary artery disease. Hippocrates wrote "Sharp pains irradiating soon toward the clavical and towards the back are fatal."[2,5] He also wrote that "Those who are constitutionally very fat are more apt to die quickly than those who are thin."[2,6] He also wrote that "Frequent recurrence of cardialgia in an elderly person, announces sudden death."[2,7] Leonardo da Vinci (1452-1519) is credited with doing the first autopsy of a victim of sudden death due to coronary artery disease; he stated that this was done when he observed the death of a hundred year old man to find "the cause of so peaceful a death".[2,8] In 1612, Paolo Grassi from Corregio, Italy described the syndrome of sudden death and listed risk factors including obesity and sedentary life style.[2,9] In 1706, Pope Clement XI commissioned Lancisi to perform autopsies in Rome of the large number of sudden deaths. Lancisi established the link of coronary heart disease and sudden death and reemphasized the relationship of Hippocrates between pain, dyspnea, and sudden death. Lancisi also identified risk factors for sudden death including smoking, urban pollution, and eating chocolate.[2,10] Many of the other notable physicians from the past have also contributed to the literature on sudden death. A brief historical review with many quotes is covered by Sidney Goldstein et al in reference number two.

Definitions

Sudden cardiac death -	unexpected death due to cardiac disease within one hour of the onset of symptoms (these may be divided into three different groups — those with no known pre-existing cardiac disease, those with known pre-existing cardiac disease that was not debilitating, and those with debilitating, pre-existing cardiac disease).
Sudden death -	unexpected death within 24 hours of the onset of symptoms due to any cause.
Out-of-hospital death -	death occurring outside of the hospital, both expected and unexpected; these include deaths occurring in hospice programs and in nursing homes.

ED death - deaths occurring in the emergency department, both expected and unexpected; these may include deaths occurring in hospice programs and in nursing homes that were transported to the emergency department.

Hospital death - Deaths occurring in the hospital; may include both sudden and expected deaths.

Out-of-hospital cardiac arrests - Patients to whom emergency medical services (paramedics or EMTs) responded; some did not have CPR begun and others may have had CPR begun. These include traumatic and non-traumatic etiologies; most are sudden deaths but may include some expected deaths.

Medical CPR - Out-of-hospital cardiac arrest cases in which CPR was begun excluding trauma and obstetrical.

Cardiac CPR - Out-of-hospital cardiac arrest cases in which CPR was begun presumed to be cardiac.

Incidence

Determining the incidence of sudden cardiac death is a complex challenge. There is no consistent database that can be examined and followed to obtain an accurate picture. Therefore, multiple databases with different definitions must be used to try and obtain different insights into the incidence of sudden cardiac death. Since between 65% and 80% of adults over the age of 35 with sudden cardiac death have coronary artery disease, the incidence of death from coronary artery disease is a good starting point. Figure 1 shows the incidence of age adjusted deaths from coronary heart disease for the 29 industrialized countries that was reported for the year 1986.[11] The data was obtained from the World Health Organization for the NHLBI report. The incidence of coronary heart disease mortality varies by more than 10 fold in the 29 industrialized nations. Though there might be some differences due to reporting from one country to the next, these variations are real. The variations are backed up by most of the medical literature that points out that there are major differences in mortality from one region to the next. The magnitude of the variations has significance in the interpretation of clinical data. For example, the recent West of Scotland trial looked at the effect of pravastatin on the mortality of men with hypercholesterolemia.[12] This data strongly suggested that mortality could be markedly reduced by treating hypercholesterolemia with pravastatin. However, the mortality in Scotland from coronary heart disease is almost twice the mortality in the United States. If there were no other factors involved, this means that in the United States, we would have to treat twice as many patients to save a life as they did in Scotland. Thus, our costs would be twice what many of the estimates of the cost per life saved would show. This does not take into account the reasons for the differences in mortality between Scotland and the United States. Maybe more of the Scottish males have hypercholesterolemia and the reason for the

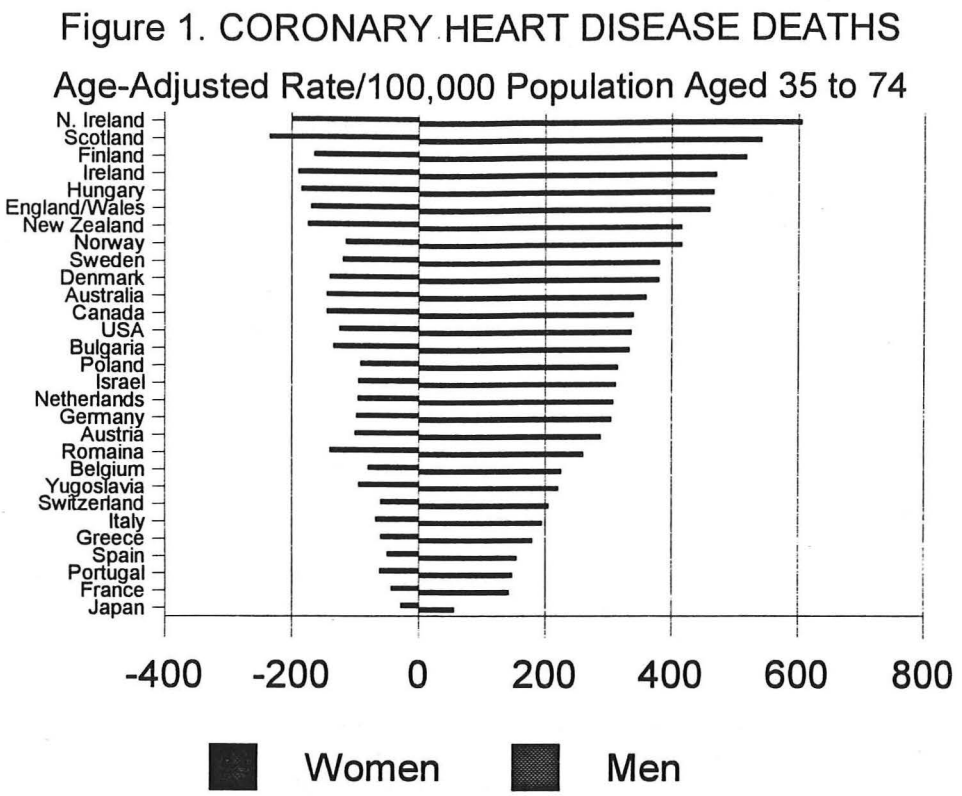

Figure 1 Morbidity and Mortality Chartbook on Cardiovascular, Lung, And Blood Disease/1990. USPHS, 1990.

differences is purely hypercholesterolemia; if this is so, then the data may be directly referable to similar hypercholesterolemia patients in the United States. However, if the differences were due to a different incidence of smoking, the data might not be as applicable for the American population. Since we do not fully understand the reasons for these regional differences, we must be careful in drawing conclusions. Most of the major clinical trials which showed reductions in cardiovascular mortality occurred in countries that have the highest mortality rates from cardiovascular disease.

The differences in mortality may represent differences in risk factors, differences in genetic predisposition, and other factors related to coronary heart disease. Some of the differences are not due to cardiovascular disease at all. In industrialized countries, people generally die of cardiovascular disease, cancer, trauma, or infection. If a country has a high premature mortality from cancer such as Japan, many individuals die of cancer before they have the opportunity to die of cardiovascular

disease. If a country has a high traumatic death rate such as the United States, then there are large numbers of individuals who will not die of cardiovascular disease. Though age-adjusting mortality attempts to balance some of these factors, they still have a major influence on mortality rates.

Table 1. Sudden Cardiac Death Age-Adjusted Mortality in Selected Countries outside of the United States

Country	Dates	Ages	Deaths of Men/ 100,000 Population	Deaths of Women/ 100,000 Population
Finland[13]	1966-79	40-59	420	
N. Karelia, Finland[14]	1975	35-64	320	40
N. Karelia, Finland[14]	1978	35-64	280	30
Beijing[15]	1974-80	≥ 30	20 (not age-adjusted)	
Auckland, NZ[16]	1981-82	25-69	190	49
Denmark[17]	1982	≥ 25	212 (not age-adjusted)	112 (not age-adjusted)

According to the World Health Organization, about 40-50% of the coronary heart disease deaths are sudden out of the hospital events. If this is true, then there is a marked variation in the incidence of sudden cardiac death. The limited amount of data that has been published outside of the United States on the incidence of sudden cardiac death shows marked variation (Table 1).

In the United States there is also variation from state to state in both the death rate from coronary heart disease and the incidence of sudden cardiac death. Gillum has reported that the percentage of coronary deaths that are sudden varies markedly from 49.6% to 70.4% in a study of 40 states.[18] Table 2 shows some of the variations that have been seen in the United States.

Table 2. Sudden Cardiac Death Age-Adjusted Mortality in the United States

Location	Dates	Ages	Deaths of Men/ 100,000 Population	Deaths of Women/ 100,000 Population
Tecumseh[19]	1959-65	≥ 30	200 (both sexes)	
Nashville[20]	1967-68	≤ 75	155 (both sexes)	
Mineapolis-St. Paul[21]	1980	30-74	244	70
Albany-Framingham[22]	1975	45-74	235	
Worcester[23]	1984	≥ 25	148 (both sexes)	
40 states[18]	1985	35-74	191	57

This data looks at out-of-hospital and emergency department deaths. Some of these deaths were expected deaths in terminally ill cardiac patients and are not truly sudden cardiac deaths. The figure of 191 deaths per 100,000 for men and 57 deaths per 100,000 for women from the 40 state study by Gillum is accepted as the best number for the United States though it includes both out-of-hospital and emergency department deaths.[18] Two studies have looked at the incidence of sudden cardiac death excluding prior coronary heart disease. From Framingham in the era of 1948 to 1974, the rate was 151 per 100,000 for men and 53 per 100,000 for women excluding prior coronary heart disease.[24] From 1970 the rate in Rochester was 79 per 100,000 for both sexes combined excluding prior coronary heart disease.[25] One standardized study looked at white males between the ages of 55 and 64 years in a systematic approach as shown in Table 3.[18]

Table 3. Standardized mortality ratios for ischemic heart disease for white males age 55-64[18]

State	Total Coronary Heart Disease	Out of hospital and ER
New York	1.259 (1)	1.223 (1)
New Jersey	1.115 (2)	1.067 (7)
Rhode Island	1.107 (3)	1.014 (14)
Michigan	1.097 (4)	1.147 (3)
South Carolina	1.079 (5)	1.116 (4)
Ohio	1.060 (6)	1.096 (5)
North Carolina	1.045 (7)	1.031 (12)
Indiana	1.043 (8)	1.049 (9)
Maine	1.027 (9)	1.066 (8)
Illinois	1.024 (10)	1.037 (10)
Georgia	1.017 (11)	1.009 (16)
Kentucky	1.016 (12)	1.014 (15)
West Virginia	1.006 (13)	1.009 (17)
Tennessee	0.995 (14)	0.968 (19)
Pennsylvania	0.995 (15)	1.021 (13)
Mississippi	0.993 (16)	0.850 (33)
Louisiana	0.988 (17)	0.942 (21)
Wisconsin	0.987 (18)	1.166 (2)

State	Total Coronary Heart Disease	Out of hospital and ER
Missouri	0.955 (19)	0.919 (24)
Virginia	0.954 (20)	0.927 (23)
Oregon	0.950 (21)	1.094 (6)
Iowa	0.940 (22)	1.000 (18)
Kansas	0.933 (23)	0.915 (25)
New Hampshire	0.929 (24)	0.911 (26)
Nebraska	0.919 (25)	0.863 (31)
Vermont	0.900 (26)	1.036 (11)
South Dakota	0.895 (27)	0.875 (28)
North Dakota	0.895 (28)	0.942 (20)
Florida	0.891 (29)	0.838 (35)
Arkansas	0.885 (30)	0.774 (38)
Nevada	0.884 (31)	0.930 (22)
Wyoming	0.846 (32)	0.887 (27)
Minnesota	0.844 (33)	0.852 (28)
Arizona	0.836 (34)	0.841 (34)
Washington	0.811 (35)	0.760 (39)
Colorado	0.793 (36)	0.870 (30)
Alaska	0.785 (37)	0.874 (29)
Idaho	0.771 (38)	0.831 (36)
Montana	0.759 (39)	0.822 (37)
Utah	0.717 (40)	0.747 (40)
Hawaii	0.605 (41)	0.599 (41)
New Mexico	0.592 (42)	0.513 (42)

The numbers represent a standardized mortality ratio with average for group being 1.000. The number in parentheses is the rank order for that column. Note that the two columns correlate for the

most part; however, there are some striking exceptions such as Wisconsin and Oregon. Though there is a tendency for mountain states and those around the great lakes to have higher mortalities, a bordering state may be on the opposite end of the spectrum.

The incidence of coronary heart disease has been declining since 1963 and since sudden cardiac death is related to the incidence of coronary heart disease, the incidence of sudden death is also believed to be declining. Four studies have looked at the incidence of sudden death using the same criteria in the same communities over time. These are shown in figures 2, 3, 4, and 5.

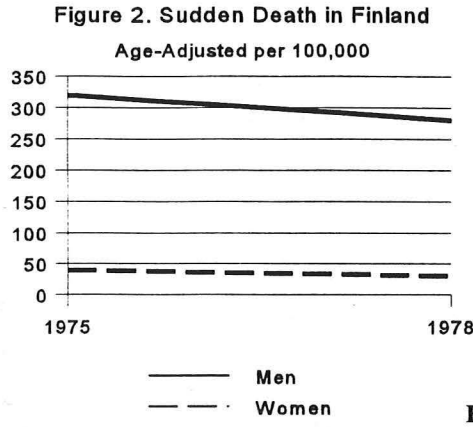

Figure 2 Salonen JT: Ann NY Acad Sci 382:423, 1982.

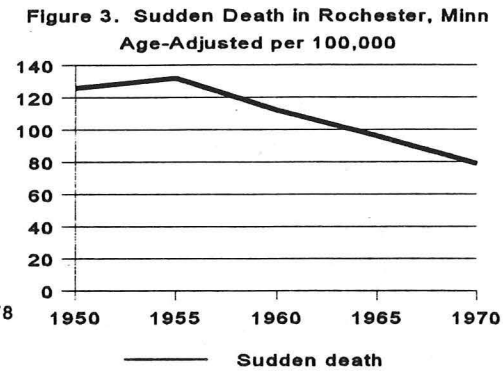

Figure 3 Elveback LR et al: Mayo Clin Proc 56:655, 1981.

Out-of-hospital deaths makes up the majority of coronary heart disease deaths in men. Most of the studies have shown that in men the percentage of sudden deaths ranges from 46.6% to 66.7% with majority being about 60%.[13-23] Women have a slightly smaller percentage of their coronary heart disease deaths being out-of-hospital ranging 5 to 10% less than men in the same study populations. Hence women appear to have a lower incidence of sudden death from coronary heart disease and to have a higher percentage of deaths in the hospital. This could be due to the higher mortality in women with myocardial infarction in the hospital, a higher incidence of congestive heart failure, and the older age of women when they have coronary heart disease. One striking difference between men and women is the percentage having prior known coronary heart disease. In most studies, women have half the incidence of known coronary heart disease at the time of their death than men.[18,21]

In order to understand the reasons for these variations in the incidence of sudden cardiac death, one must analyze many different factors. Sudden cardiac death is very complex and depends

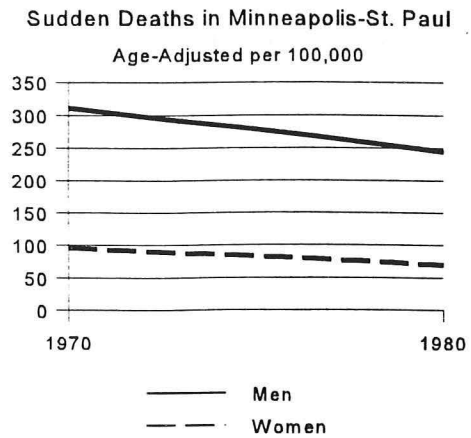

Figure 4 Gillum RF et al: N Engl J Med 309:1353, 1983.

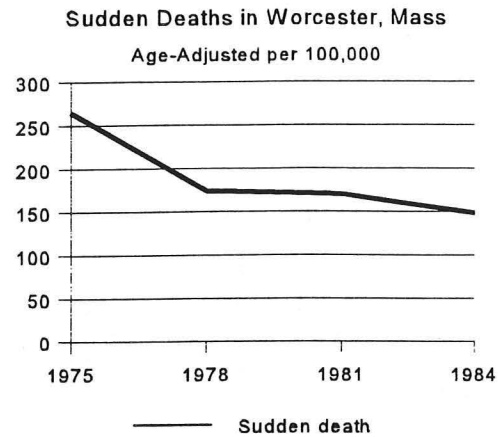

Figure 5 Goldberg RJ et al: Am Heart J 115:751, 1988.

upon three major sets of factors interacting together to cause sudden cardiac death. The first is the disease process. Each disease process has different risks of developing sudden cardiac death. The major etiologies of underlying diseases that can precipitate sudden cardiac death will be discussed first. The second major groups of causes is left ventricular dysfunction and the many different variations of left ventricular dysfunction. The third major group is the arrhythmia and it various triggers. To understand sudden cardiac death one must understand each of these groups and the many variations. This makes the prediction of sudden cardiac death very difficult. Therapy and prevention of sudden cardiac death therefore becomes very difficult.

Causes of sudden death

Before discussing cardiovascular causes of sudden cardiac death, it must be recognized that there are also many non-cardiac causes of sudden death. The causes vary by age. The many non-cardiac causes include traumatic etiologies and medical etiologies such as respiratory disease, gastrointestinal disease, urinary disease, neurologic disease, infection, and drugs either as an overdose or an idiosyncratic reaction to the drug. When you exclude traumatic causes, medical conditions other than cardiac cause sudden death in between 20 and 40% of victims. If you evaluate series of patients since 1960 the percentage of adults having a cardiac etiology varies from 63.9% to 78.5% with the majority of series reporting about 70%[17,26-30] In the Baltimore study, respiratory disease was 5.9%; while in Europe and Japan respiratory disease ranged from 4.6-17.7%.[17,26-30] There is a general feeling that the percentage of deaths due to respiratory disease has risen in the last 30 years to about 10% in the United States but there is not a good pathologic series that has been done since the Baltimore study.[26] In the Baltimore study, cerebral causes accounted for 11.5% of the sudden deaths; while in Europe and Japan, cerebral causes accounted for between 3.8% and 16% with Japan being

the leader in this cause.[17,26-30] Digestive diseases accounted for about 2 to 5% of the cases.[17,26-30] Other causes including urinary and infectious causes ranged from 2% abroad to 17.9% in Baltimore.[17,26-30] In younger patients aged 20 to 45 years, the causes of natural sudden death were circulatory in 38%, central nervous system in 22%, respiratory in 18%, gastrointestinal in 13%, urinary tract in 4%, and miscellaneous in 5%.

In Dallas, Dr. Zachariah and I analyzed the data from the Dallas Fire Department Emergency Medical Service System for the years 1994 and 1995. The data is shown in Table 4. As can be seen from this data, there are a significant number of traumatic events totaling 438 cases. Trauma comprises 18.3% of the victims on whom CPR was begun by the fire department. Presumed non-cardiac causes accounted for 32% of the victims on whom CPR was begun and 49.6% of the victims were presumed to be cardiac. If you exclude trauma, then cardiac patients make up 60.8% of the CPR population. However, the group of individuals under 35 years of age have a very high incidence of non-cardiac medical causes and trauma. As you get older trauma and non-cardiac causes diminish between ages 35 and 65. Over the age of 65 non-cardiac causes again rise.

Table 4. Causes of cardiac arrest responses by the Dallas Fire Department - 1994-95

	Number of events
Total cardiac arrest dispatches	**3274**
No CPR (Rigor mortis, etc.)	**887**
Total with CPR	**2387**
Gun shot wounds	**162**
Stab wounds	**19**
Motor vehicle crashes	**179**
Other trauma	**54**
Burn	**5**
Drowning	**16**
Obstetrical	**3**
Total Medical CPR	**1949**
Presumed cardiac	**1185**
Presumed non-cardiac	**764**
Total ventricular fibrillation	**645**

Coronary Heart Disease

Underlying Disease - Of those patients with a cardiac cause of sudden cardiac disease, coronary heart disease is by far the most prevalent cause. Since it is the most prevalent cause of sudden cardiac death, the risk factors for coronary heart disease become the major risk factors for sudden cardiac death. The classical risk factors include hereditary, age, sex, cholesterol, elevated LDL-cholesterol, reduced HDL cholesterol, hypertension, smoking, diabetes mellitus, lack of exercise, and obesity[31]. However, these risk factors only account for some of the variations. Many new risk factors have been identified. A recent NIH grand rounds suggested adding a few additional risk factors to the list. This expanded list includes the currently identified risk factors plus the proatherogenic risk factors of homocysteine, lipoprotein particle oxidation, hyperinsulinemia, lipoprotein particle subspecies, apolipoprotein E isoforms, cholesteryl ester transfer protein, the prothrombogenic risk factors of plasminogen, fibrinogen, Factor VII, plasminogen activator inhibitor 1, lipoprotein (a), and the antiatherogenic risk factors of apolipoprotein A-I, lecithin-cholesterol acyl transferase, hepatic lipase, low-density lipoprotein receptor, very low-density lipoprotein receptor, and apolipoprotein E.[31] Thus, there are many factors that can influence the incidence of coronary heart disease. Each of these factors can therefore influence the incidence of sudden cardiac death.

Victims of sudden cardiac death have a mixture of one, two, three vessel disease and a small incidence of left main coronary artery disease. The distribution of coronary artery disease does not differ between patients with angina pectoris, myocardial infarction, unstable angina, or sudden cardiac death.[32-42] The severity of the stenosis also is not important in differentiating the different syndromes.[32-33] Prior myocardial infarction was also not important in differentiating the different syndromes. [32-42] Thus, the different syndromes do not differ in the anatomy of the coronary arteries nor the presence of scar.

The relationship of myocardial infarction with sudden cardiac death has been very confused for centuries. After Leonardo da Vinci established the relationship between coronary heart disease and sudden cardiac death, it was assumed that myocardial infarction caused sudden cardiac death. It was felt that every case of sudden cardiac death was due to myocardial infarction and that every case of myocardial infarction caused sudden cardiac death.[2] It was James Herrick in 1912 who showed that myocardial infarction did not always result in sudden death; in fact, most patients with myocardial infarction survived.[43] It was 20 years before the medical community accepted Herrick's work and hypothesis.[2,44] After it was agreed that most patients survived an acute myocardial infarction, it was still felt that all sudden cardiac death was due to myocardial infarction and the problem was the inability of pathologic techniques to recognize infarction in the first few minutes. When groups of patients were analyzed for the presence of coronary thrombosis from the time of onset of symptoms, it was noticed that those who died instantly rarely had coronary thrombosis; while, the percentage of patients with coronary occlusion increased for most of the first 24 hours.[34,45-46] Since it was felt that all victims of sudden cardiac death with coronary artery disease had myocardial infarction, the hypothesis was raised that coronary thrombosis was a secondary phenomena.[34,45-46] This hypothesis felt that myocardial infarction was due to ischemia induced by the coronary plaque and this ischemia became irreversible causing cell death. When myocardial cell died

in a zone, they would swell. This swelling caused edema which limited coronary flow. Diminished coronary flow over time caused the coronary to thrombose.

Figure 6. ECG Changes in Survivors of Out-of-hospital Ventricular fibrillation n = 239

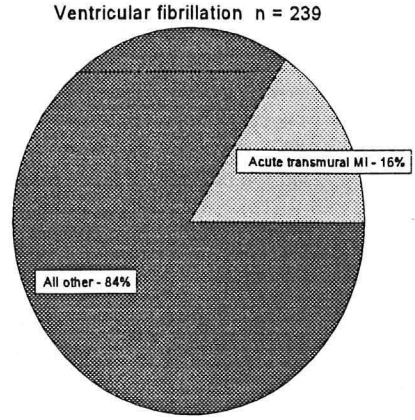

Figure 6 Cobb LA et al: Circulation 51, 52:III-223, 1975

Figure 7. Incidence of Necrosis in Surivors of Ventricular Fibrillation n = 175

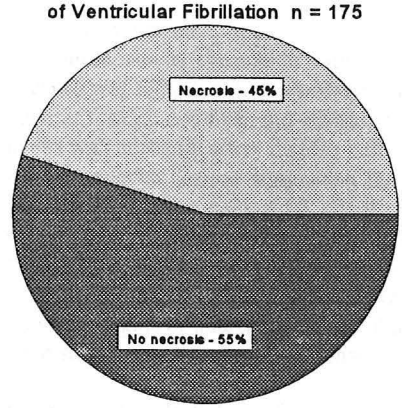

Figure 7 Cobb LA et al: Circulation: 51,52:III-223, 1975

This theory of secondary thrombosis began to unravel with the work of Leonard Cobb and others.[47] When Cobb looked at patients who were successfully resuscitated by the Seattle Fire Department, he found that most of them had no evidence of transmural myocardial infarction using serial ECG changes (Figure 6).[47] Thus, most patients did not have transmural myocardial infarction. He then looked at enzyme evidence of necrosis and again found that most patients did not have evidence of necrosis (Figure 7).[47] This finding changed our impression of what was happening in sudden cardiac death. Since few of the patients showed evidence of transmural infarction and the minority of patients showed evidence of necrosis by enzyme evidence, another explanation was needed for the patients that did not have necrosis. As these patients had a great deal of complex ventricular arrhythmias, the PVC theory was born for the etiology of these patients with sudden cardiac death. The PVC theory flourished and many new antiarrhythmic agents were developed and patients were risk stratified post myocardial infarction with Holter monitoring. Complex workups of ventricular ectopy developed and became widespread until the CAST trial was released and it was shown that treating PVCs was not beneficial but harmful.[48]

In 1989 Davies and Thomas published a landmark study that began to focus our understanding of sudden cardiac death (Table 5).[49] Prior to this study several studies had suggested that ischemia played an important role in sudden cardiac death.[33,50-51] This was followed by studies that showed that platelet aggregates were also involved in the process of sudden cardiac death.[52-53] The work of Davies and Thomas and that of Roberts showed that there was plaque fissuring in patients with sudden cardiac death similar to what has been described with unstable angina

pectoris.[54-56] Davies and Thomas compared sudden cardiac death with two different control groups. The first was a group of patients with atheromas who died of non-cardiac diseases and are labeled in Table 5 as atheroma-basal control. The second control were patients dying of atheroma related disease but not with sudden cardiac death. The fact that mural coronary thrombi and occlusive thrombi were seen predominantly in the group with sudden cardiac death shows that unstable plaque is the most common cause of sudden cardiac death[49]. This explains why many of the patients had reported chest pain in the two weeks prior to their sudden cardiac death and why many of them had seen a physician in the last two weeks. Thus, from these studies it is apparent that the problem is plaque rupture or fissuring that leads to thrombus formation either mural thrombus in the coronary artery or an occlusive thrombus. The percentages agree with many prior studies of resuscitated victims in that most victims do not have myocardial infarction.

Table 5. Distribution of Vascular Events in Sudden Ischemic Death[49]

	Atheroma-Basal Control	Related Control	Study Patients
No acute arterial lesion	91.3%	78.3%	19%
Plaque fissure alone	8.7%	16.7%	7.7%
Mural thrombus	0	5%	43.5%
Occlusive thrombus	0	0	29.8%

These findings have been challenged by Kragel and Roberts who found a similar 29% incidence of intracoronary thrombi in both unstable angina pectoris and sudden cardiac death and a higher percentage of 69% in patients with an acute myocardial infarction.[57] Very recently Spaulding studied patients resuscitated from out-of-hospital cardiac arrest with angiography and found that 40 of 60 patients with coronary artery disease had occlusions of their coronary arteries and many of the rest had very irregular lesions suggesting mural thrombi.[58] Spaulding reported that many of the patients did not have chest pain or ST elevation. Though there is debate on the exact incidence of plaque rupture and thrombus in the coronary arteries, it is apparent that the syndrome of sudden cardiac death in the presence of coronary artery disease is a aliquot of patients with unstable angina and myocardial infarction. Thus, the initiating cause of many cases of sudden cardiac death is the onset of unstable angina or infarction. If unstable angina or myocardial infarction occurs in the right setting, then sudden cardiac death may ensue.

Sudden cardiac death has a Circadian rhythm peaking around 9 AM. There is also a second peak in the afternoon. When you correct this for awakening times, it is apparent that it is not a true Circadian rhythm but rather a relationship to arousal.[59-61] It appears that this correlates with a diurnal or arousal relationship to circulating norepinephrine. Circulating levels of norepinephrine, heart rate, blood pressure, platelet activation,, and decreased fibrinolytic activity all have the same variation [62-63]

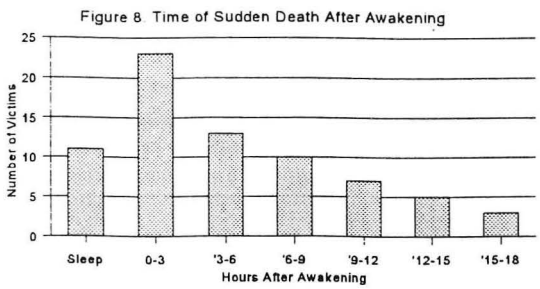

Figure 8 Willich SN et al: Am J Cardiol 70:65, 1992

One interesting variation is the Spanish Trial on Sudden Death; this trial showed that there was a diurnal variation similar to other trials but in the afternoon there was a second higher peak following siesta.[64] The one study that looked at the diurnal variation of ventricular fibrillation during Holter monitoring failed to find any variation.[65] This also suggests that we are looking at different aspects of the same syndromes. It appears something goes wrong with the plaque such as rupture or fissuring. Platelet aggregation begins and if the vessel occludes there is usually myocardial infarction. With myocardial infarction, a patient may have a silent event, a painful event, or sudden death. If there is not an occlusive thrombus, then the patient may have unstable angina with can be silent, painful, or result in sudden death.

The clinical prodromal symptoms of sudden cardiac death varies. Only 43% of patients with sudden cardiac death had any symptoms at all.[32-33,66-69] Only 25% of patients with sudden cardiac death have chest pain, 31% have fatigue and 30% have dyspnea as prodromal symptoms.[32-33,66-69] Thirty one percent of patients have contacted their physician within two weeks of the event.[32-33,56-69] Of the patients who lasted more than one minute, their activities were normal for the day.[32] There is a subset of patients who had instantaneous sudden death without any outward sign to witnesses; this group had an increased incidence of heavy exertion or emotional conflict.[32]

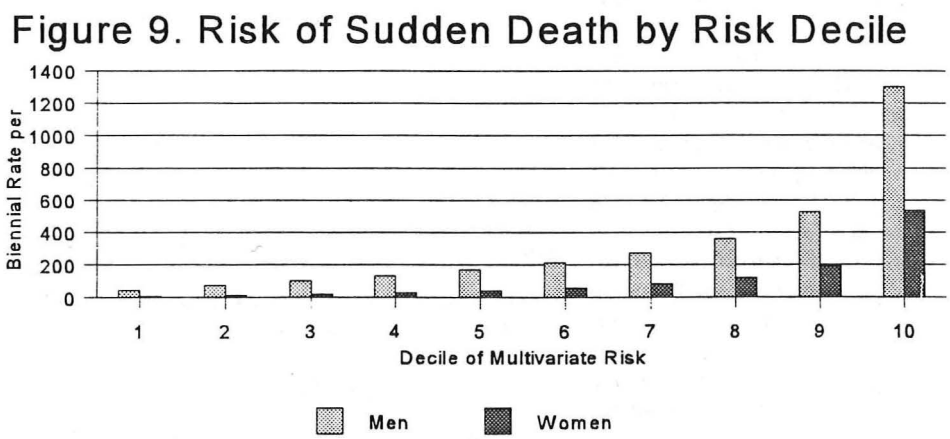

Figure 9 Kannel WB et al: Drugs 18(suppl):1, 1984.

Figure 9 shows the effect of multivariate risk on sudden death mortality in coronary heart disease.[70] The variables used in this multivariate risk analysis include age, systolic blood pressure, serum cholesterol, vital capacity, cigarettes per day, relative weight, and heart rate.[70] Thus, not only does the risk increase with each risk factor for coronary heart disease but there is marked interplay between risk factors. Hypertension is obviously a risk factor for coronary heart disease, but hypertension also increases the risk of sudden death in the presence of coronary heart disease. Therefore, risk factors are doubly important.

Functional component - The second major determinant of the outcome in a patient with coronary heart disease is left ventricular function. In patients with coronary heart disease, depressed left ventricular function and heart failure are potent markers for sudden cardiac death.[71-74] Activation of the renin-angiotensin system also markedly increases risk in these patients. Other markers of left ventricular abnormalities including scarring, ventricular aneurysms, and left ventricular hypertrophy also markedly increase the risk of sudden cardiac death.[75-79] Left ventricular dysfunction is a marked predictor of sudden cardiac death. Mild decreases in ejection fraction (40%) more than doubles the risk of sudden cardiac death; with decreasing ejection fraction the rate of sudden cardiac death rises exponentially. However, other markers of abnormal ventricular function also markedly increase risk. The presence of left ventricular hypertrophy with preserved ventricular function markedly increases cardiovascular risk. Increases in end-diastolic volume or end-systolic volume also increase the degree of risk. In patients who have ventricular scarring from infarction, the larger the scar the greater the risk of sudden cardiac death presumably from macro-reentrant pathways; the risk is even greater if the scar forms a left ventricular aneurysm.

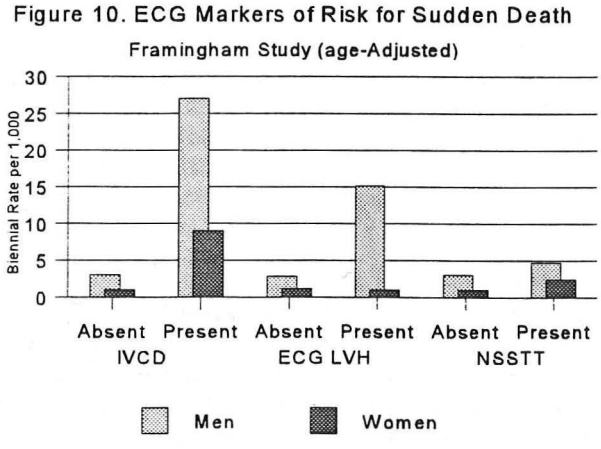

Figure 10. ECG Markers of Risk for Sudden Death

Figure 10 Kannel WB et al: Drugs 28(suppl):1, 1984.

The functional component also includes electrocardiographic criteria (Figure 10).[70] The presence of bundle branch blocks increases the risk 9 fold in both men and women. The presence of LVH on the electrocardiogram increases the risk 5 fold in men but not in women. This finding in women is probably due to a small sample size. LVH is a risk factor for total mortality in women but sudden cardiac death remains unclear. Even non-specific ST and T wave changes are a risk factor for sudden cardiac death. Therefore, abnormal function as defined by the resting ECG is a predictor of sudden cardiac death having a major influence on mortality. Signal averaged electrocardiograms are also a predictor that increases the odds ratio for sudden cardiac

death.[81-86] An abnormal signal-averaged electrocardiogram increased the odds ratio 11 fold over a normal signal-averaged electrocardiogram in patients post myocardial infarction; this was the odds ratio for ventricular tachycardia or sudden cardiac death.[84] Signal-averaged electrocardiograms also predicted marked increased risk in patients with hypertrophic cardiomyopathy and non-ischemic congestive cardiomyopathy.[87-88]

Other functional abnormalities are also important. The presence or absence of ischemia or injury is also a very powerful predictor of sudden cardiac death. Coronary angiographic studies also determine the risk of sudden cardiac death. The greater the number of vessels involved the greater is the risk for sudden cardiac death, with main left coronary lesions increasing the risk more; add a reduced ejection fraction and the risk is even higher for any given number of vessels involved.[89-92] Exercise testing on the treadmill is also a major predictor of the risk of sudden cardiac death. Patients who must terminated the test in the first 6 minutes of a Bruce protocol have a 15-20% annual mortality as compared to 2% for those who complete 12 minutes.[93-94] Exercise thallium scintigraphy and radionuclide ventriculography also identify groups of patients who have poor prognosis, including reversible ischemia, large areas of poor uptake, multiple areas of poor uptake, poor left ventricular function, and decreased regional function.[95-100] Echocardiography can also divide patients into high and low risk with either resting studies or exercise or stress studies.[101-103]

The various clinical syndromes also affect the outcome of patients. When a patient has coronary artery disease, any of the major clinical syndromes also increases the likelihood of sudden cardiac death. This has been shown in patients with stable angina pectoris, unstable angina pectoris, acute myocardial infarction, and silent ischemia.[104-109]

Arrhythmic triggers - The presence of ventricular arrhythmias has long been known to be associated with an increased risk of sudden death. The MILIS trial evaluated post myocardial infarction patients prior to discharge with a Holter monitor.[100] They found that if a patient had no ventricular ectopy, their annual risk was 1%. The presence of as few as 10 unifocal PVCs per hour increased the risk to 2% annual risk. If the patient had complex ectopy, then the mortality increased to 5% annual risk. Thus, both frequency and complexity of PVCs increased the risk of sudden cardiac death. This led to the treatment of PVCs with antiarrhythmic agents until the Cardiac Arrhythmia Suppression Trial (CAST) which showed that eliminating PVCs did not decrease risk but paradoxically increased risk.[110]

Autonomic dysfunction has also been identified as a predictor of patients with sudden cardiac death. The lack of sinus arrhythmia (loss of RR variability) has been identified as a factor that predicts risk of sudden cardiac death.[111] Baroreceptor insensitivity has also been shown to be a predictor.[112-113] Autonomic reflexes due to diving, cold pressor, and psychological stress have been implicated in cases of sudden cardiac death.[2] When Friedman evaluated patient who dropped dead without any warning signs at all, psychological and physical stress were a major determinant.[32]

Torsade de pointes and ventricular fibrillation have been associated with prolongation of the QT interval.[2] Prolongation of the QT interval can be acquired, congenital, or associated with drugs.

Acquired long QT intervals can be due to electrolyte disturbances such as hypokalemia and hypomagnesemia. Severe bradycardia due to complete heart block, sinus node dysfunction, or ventricular bigeminy (causing a relative slowing of the conducted beat). Toxins including cocaine, arsenic, and organophosphate insecticides have been described. Cardiac disorders including myocarditis and ventricular tumors are reported. Endocrine disorders have also been shown to prolong the QT interval such as hypothyroidism, pheochromocytoma, and hyperaldosteronism. Subarachnoid hemorrhage, CVA's and encephalitis are intracranial causes. Nutritional disorders of starvation and liquid protein diet have been shown to prolong the QT interval. Inherited disorders of the QT interval also can cause sudden death; these include Jervell and Lange-Nielsen syndrome (associated with deafness) and the Romano-Ward syndrome. Drugs have also been implicated. Antiarrhythmic agents both class IA and III are well recognized as causes. The antianginal agents -- bepridil, lidoflazine, and prenylamine — have been shown to cause sudden cardiac death. The psychotropic agents phenothiazines and haloperidol can cause QT prolongation. Antidepressant agents, both the tricyclic and tetracyclic agents, have been implicated. Antimicrobial therapy with erythromycin, trimethoprim-sulfamethoxazole, pentamidine, amantidine, and cloroquine can also cause torsade. The antifungals, ketoconazole and itraconazole, have similar tendancies. The antihistaminics, terfenadine and astemizole can also cause torsade. Additional drugs include the antihypertensive agent ketanserin and the hypolipidemic agent probucol. Not only do each of these conditions or agents independently cause torsade de pointes or ventricular fibrillation, combinations of factors or drugs cause a marked increased in risk as exemplified by the combination of Seldane and erythromycin.

Therefore, the cause of sudden cardiac death in a patient with coronary artery disease is very complex with an interplay between the underlying disease, functional components, and arrhythmic triggers. Some factors may influence each component. If you examine the role of hypertension, it is obviously a risk factor for coronary artery disease. Hypertension also decreases ejection fraction by increasing afterload. The ventricle frequently becomes hypertrophied from the hypertension and may increase its end-diastolic volume. Hypertension also affects the baroreceptors decreasing the heart rate, making the baroreceptors less sensitive, and decreasing the RR variation. Therefore, hypertension influences the risk of sudden cardiac death in many different manners. Lipid abnormalities are also complex. A recent study by Burke et al[114] found that patients who had a high total cholesterol to HDL-cholesterol ratio had a marked increase in plaque rupture in patients with sudden death. They also found that patients who were smokers had more acute thromboses. Thus, lipid abnormalities may predispose to plaque rupture and smoking may predispose to thrombosis as well as being risk factors. There may also be major interplay between the variables. If a patient has a high cholesterol to HDL level and smokes, then the cholesterol might predispose to plaque rupture that then clots due to the smoking predisposition.[114]

Drugs that Alter Mortality after Infarction

There have been many trials looking at various agents after myocardial infarction. Some of these agents have had effects on mortality and sudden death but others have not. One recent review will be summarized (Table 6).[115] Beta blocking agents have been shown to be very effective. Beta blocking agents that have had a marked effect are metoprolol, propranolol, timolol, and acebutolol;

several other beta blocking agents have not been nearly as protective. All of the ACE inhibitors that have been studied seem to be protective in patients with left ventricular dysfunction. Calcium channel blockers do not appear to be effective as a class. Verapamil and diltiazem appear to cause harm in people with evidence of left ventricular failure while they appear to be beneficial in patients with normal left ventricular function. Short acting nifedipine also appears to do harm. There are not studies of other calcium channel blocking agents. Of the antiarrhythmic agents, only amiodarone appears to have benefit; however, the studies are weaker than for some of the other agents.

Table 6. Meta-Analyses of Randomized Trials of Drug Therapy Administered After Myocardial Infarction

Drug Class	No. Of Trials	No. Of Patients	Relative Risk of Death (95% CI)
Beta blockers	26	24,298	0.77 (0.70-0.84)
ACE inhibitors	3	5,986	0.78 (0.70-0.86)
Ca channel blockers	24	20,342	1.04 (0.95-1.14)
Class I antiarrhythmic	18	6,300	1.21 (1.01-1.44)
Amiodarone	9	1,557	0.71 (0.51-0.97)

Other Cardiovascular Causes of Sudden Cardiac Death

There are many other cardiovascular causes of sudden cardiac death. Though most forms of cardiovascular disease can cause sudden death, certain causes are commonly seen. These other causes include hypertrophic cardiomyopathies, dilated cardiomyopathies, aortic stenosis, mitral valve prolapse, Wolff-Parkinson-White, and congenital heart disease.[2] Atheletes point out some of the variations at different ages as are shown in Figures 11 and 12.[116-117] As can be seen the etiology of the sudden cardiac death changes markedly with age.

Table 11. Sudden Death - Athletes

<35 years old

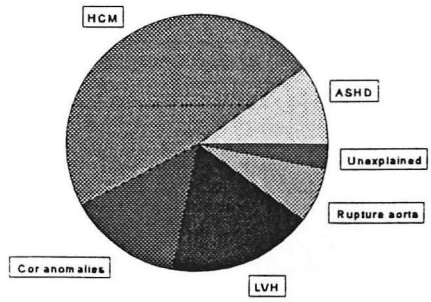

Figure 11 Maron BJ et al: Circulation 62:218, 1980.

Table 12. Sudden Death - Athletes

> 35 years old

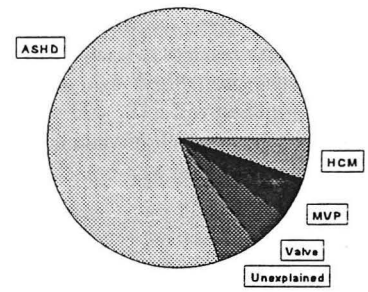

Figure 12 Maron BJ et al: J Am Coll Cardiol 7:204, 1986

Legend: ASHD = coronary heart disease, HCM = hypertrophic cardiomyopathy, MVP = mitral valve prolapse, cor anomalies = congenital coronary anomalies, LVH = idiopathic LVH

Rhythms in Patients with Sudden Cardiac Death

Figure 13. Holter Monitor Rhythms

Adults with Sudden Death

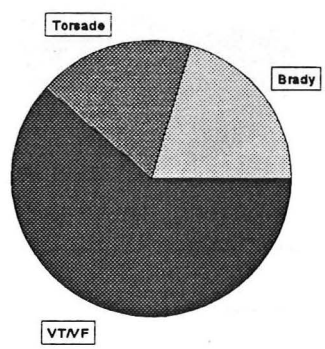

Figure 13 Bayes de Luna A: J Ambulat Monitoring 2:3, 1989.

There have been several studies that have looked at the rhythms that caused sudden cardiac death. Resuscitated survivors are not a good group to evaluate rhythms as survivors usually had witnessed ventricular fibrillation. Due to EMS response time some of the ventricular fibrillation may have deteriorated into asystole. Bayes de Luna et al reported 233 cases of sudden cardiac death while undergoing Holter monitoring (Figure 13).[118] These patients averaged 70 years of age. Eighty four percent had coronary heart disease and 12% had other forms of heart disease. Men predominated with 76% of the patients. Only in the group with torsade de pointes did women predominate (60%).

Figure 14. Pediatric Rhythms

in Sudden Cardiac Death

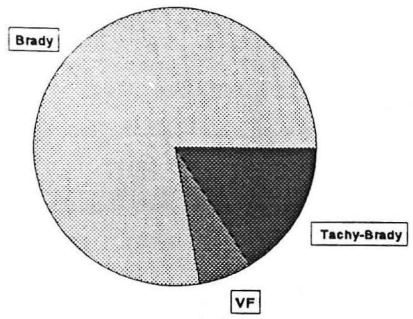

Figure 14 Walsh CK et al: Am J Cardiol 51:557, 1983.

Pediatric patients differ in the cause of the sudden cardiac arrest (Figure 14).[119] While ventricular fibrillation predominated in the adults with coronary heart disease, pediatric patients developed bradycardia or tachycardia that rapidly became bradycardia. Ventricular fibrillation was seen only in about 6%. The few pediatric patients with ventricular fibrillation had congenital heart disease and an enlarged heart.

Figure 15. Rhythms in Heart Failure

Patients with Sudden Death

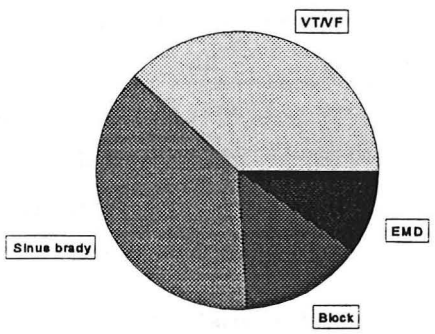

Figure 15 Luu M et al: Circulation 80:1675, 1989.

Patients with heart failure may have more bradycardia than ventricular fibrillation (Figure 15).[120] Luu et al found that patients with advanced heart failure awaiting transplantation did not commonly have ventricular fibrillation as the etiology. This group of patients frequently suddenly became bradycardic and then went into pulseless electrical activity.

Demographic Characteristics

Age - The incidence of sudden cardiac death increases markedly with age. As can be seen in Figure 16, the incidence of out-of-hospital death from coronary heart disease increases 10 fold from the 35-44 year range to the 65-74 year range in both men and women.[121]

Figure 16. Age-Specific Out-of-Hospital Deaths

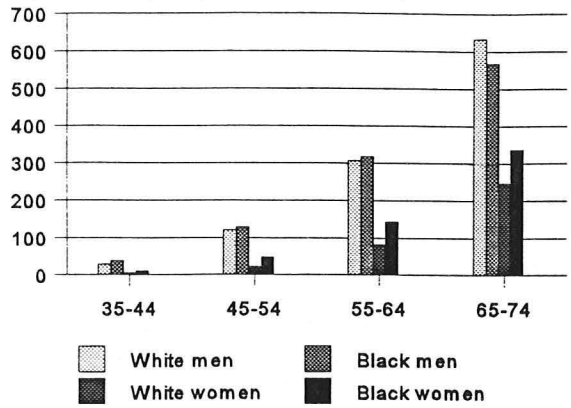

Figure 16 Gillum RF: Circulation 79,756, 1989.

Race - Ethnic differences have been minimal in most studies. Some studies have shown a slightly higher or lower rate for whites versus other races but the differences have not been consistent. Figure 16 shows the differences between the ethnic groups in the United States.[121] A recent study from New York City revealed that Blacks had a higher incidence of cardiovascular sudden deaths than whites with similar socioeconomic backgrounds.[122] In the 45-64 year age range, black men in New York City born in the south had a cardiovascular death rate of 835/100,000. Black men born in the northeast had a cardiovascular death rate of 653/100,000. While black men born in the Caribbean area had a cardiovascular death rate of 165/100,000. Therefore, there are marked differences that vary with the place of birth not race. The only racial group that is significantly different are third generation Japanese-Americans who have a much lower mortality than other ethnic groups.[123]

Table 7. Racial Differences in Dallas in Victims of Cardiac Arrest

	All	White	Afro/Amer	Hispanic	Other
# Medical CPR	1949	924	821	185	6
Cardiac/Medical	60.8%	62.9%	58.3%	52.4%	60.0%
VF/Medical CPR	33.1%	34.7%	32.6%	28.6%	40.0%
VF/Cardiac CPR	54.4%	55.0%	55.9%	54.6%	66.7%

Here in Dallas (Table 7), there does not appear to be any differences in the various ethnic groups. The white population and the African-American population of Dallas seem to have rates of cardiac arrest that approximates their percent of the population. While Hispanics appear to have a lower incidence, these numbers are not age-adjusted and the Dallas Hispanic population is much younger than the other ethnic groups. The incidence of ventricular fibrillation is almost identical in each of the various groups contrary to the impressions of many investigators.

Gender - Men have a higher incidence of out-of-hospital deaths than women. Women have a higher incidence of in-hospital deaths.[18,21] As previously stated, this may be due to a higher in-hospital mortality from acute myocardial infarction than males, older age, and a higher incidence of congestive heart failure. The Dallas data is shown in Table 8.

Table 8. Gender Differences in Dallas in Victims of Cardiac Arrest

	All	Men	Women
# Medical CPR	1949	1167	780
Cardiac/Medical CPR	60.8%	63.2%	57.3%
VF/Medical CPR	33.1%	37.9%	27.6%
VF/Cardiac CPR	54.4%	59.9%	48.1%

The age distribution of cardiac arrest handled by the Fire Department in Dallas is shown in Figure 17. When you look at all CPR's, SIDS and trauma make up many of the cases in the first decade of life. The second and third decades are dominated by trauma. After the third decade, cardiovascular disease becomes a dominant cause of death with coronary heart disease being the most common etiology. The largest number of cardiac arrest victims are between 70 and 79. Medical CPR has a similar age distribution as all CPR. Ventricular fibrillation increases and peaks earlier than medical CPR. Ventricular fibrillation peaks in the 60-69 year age range. Figure 18 shows the percent of medical CPR cases that had ventricular fibrillation. Ventricular fibrillation as a percent of medical CPR appears to increase with age to the 40-49 year age range and then declines. The high incidences in the 10-29 year age range represent very few cases. The high incidence in this age range may be from hypertrophic cardiomyopathy, long QT syndromes, and cocaine usage.

The location of the cardiac arrest is an important consideration for the location of paramedic teams and first responder defibrillation with automated external defibrillators. In the two year period, the majority of events (85%) occurred in the patient's home. Nursing homes had 245 events in two years and 13.5% were ventricular fibrillation. Large medical office complexes (more than 3 stories) had 56 events and 42.9% were ventricular fibrillation. There were 6 episodes in the jail with 3 being from ventricular fibrillation. All of the large office buildings in the City of Dallas had 40 episodes of ventricular fibrillation for the two year period; most of these were younger with the peak being in the 50-59 year range. Other locations with multiple events in a year included the airports, shopping malls, and adult book stores. The number of patients with ventricular fibrillation are about 320 per year. This has declined from over 550 cases per year in the early 1980's. Since survival from cardiac arrest is predominantly from ventricular fibrillation, this explains why the number of survivors has decreased even though technology has improved. The decreasing numbers of patients with ventricular fibrillation shows that there will be diminishing returns even with more wide-spread use of early defibrillation.

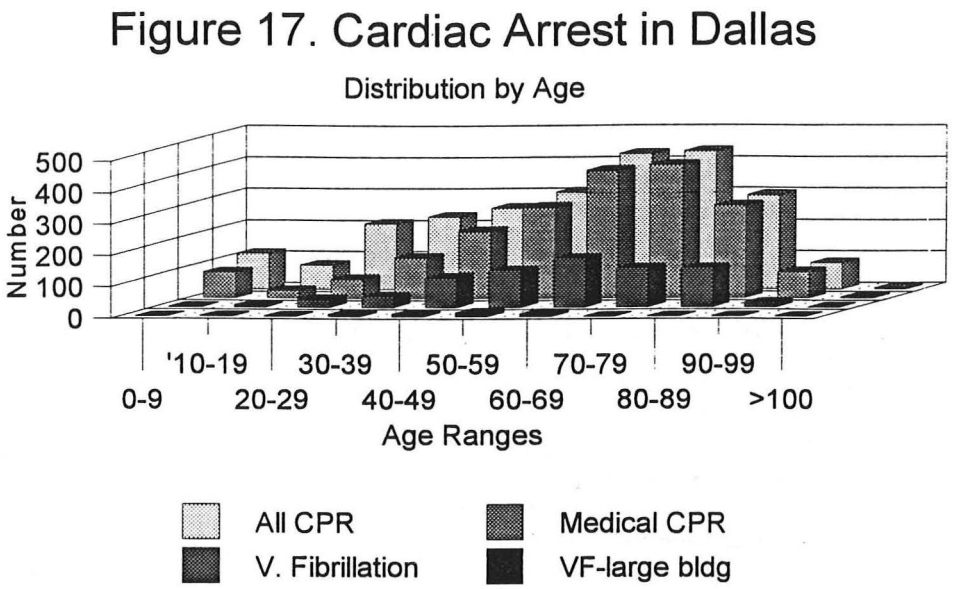

Figure 17

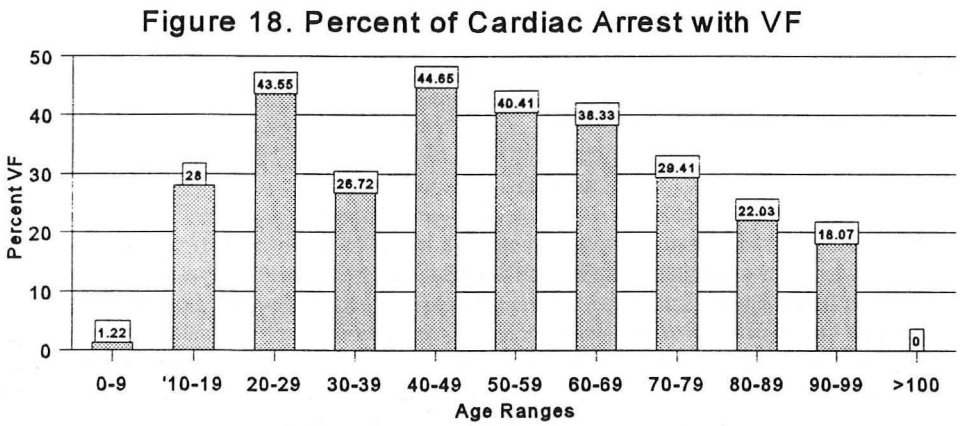

Figure 18

Water Quality

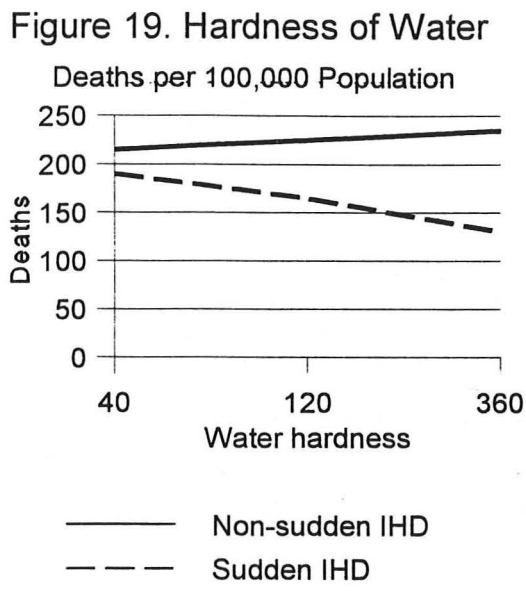

Figure 19 Anderson TW et al: In: Magnesium in Health and Disease. New York:SP Med Science Books, 1980, p 565.

One of the more unusual correlates is water hardness (Figure 19).[124] There have been a number of studies that have shown that the incidence of sudden death decreases with water hardness. Soft water increases the incidence of sudden death. Hard water decreases the incidence of sudden death and replaces it with non-sudden death. Since the major ion present in hard water is magnesium and low magnesium levels are definitely correlated with sudden cardiac death, there is a potential physiologic mechanism for this finding. It is interesting to note that some of the studies that support the routine use of magnesium in acute myocardial infarction are from locations that have soft water.

Airports and Airplanes

The management of victims of a cardiac arrest poses major challenges on airplanes. Survival from cardiac arrest decreases rapidly from the time of the event until a rhythm is restored in the patient. In general, survival without proper medical treatment is unlikely after 10 minutes and nonexistent after 20 minutes. Performing manual cardiopulmonary resuscitation (CPR) only slightly improves the results at 10 and 20 minutes. Survival from cardiac arrest is determined mostly by the time from the event until they are defibrillated or shocked for those victims in ventricular fibrillation, which is one of three different rhythms that cause cardiac arrest. If they can be defibrillated within the first minute, greater than 90% survive. If they cannot be shocked until 5 minutes, 40% survive. If they cannot be shocked until 10 minutes after the event, less than 10% survive. Thus, survival from cardiac arrest occurs when the patient has ventricular fibrillation and is defibrillated or shocked rapidly. On an airplane, an emergency diversion and landing requires at least 20 minutes with another 10-20 minutes to get the plane to where the victim can be removed by the appropriate medical personnel.[125]

Therefore, cardiac arrest on an airplane under normal circumstances is not survivable.

The incidence of cardiac arrest on commercial airplanes is extremely low, but with the enormous numbers of travelers the total is significant. In fact more people die each year of cardiac arrest on commercial airlines than die from crashes. The exact number of deaths is hard to determine. J. Crewdson of the Chicago Tribune and T. Friend of USA Today have estimated that there are up to 1,000 deaths on carriers that are members of the International Airline Transport Association (IATA).[126-127] Reports from carriers are often incomplete or underestimate the magnitude of the problem. Qantas Airlines has carefully evaluated events both on their airplanes and in their terminals. Dr. O'Rourke and his co-investigators reported this information at the American Heart Association Conference on Public Access Defibrillation II in Washington in April of 1997. From their numbers, they have estimated that the rate of events would be 311 cardiac arrests per year for all IATA carriers.[128] This is probably the best estimate that is available. This estimate is in line with many other estimates that have been made. From this estimate, the number of cardiac arrests on domestic carriers in the United States would be about 70-80 per year with 72 being the most widely accepted number.[129-137] It should be pointed out that there are almost as many cardiac arrests in the terminals as on the aircraft. At Dallas/Fort Worth International Airport, the second busiest commercial airport in the United States, there are 15 to 16 cardiac arrests per year. Half of these events occur on the aircraft and half in the terminal. Qantas reported 19 events in their terminals and 27 events on their aircraft; not all of the terminals are under Qantas control causing an under-reporting of events in terminals.

From the Qantas data presented by Dr. O'Rourke, 17 of 19 events in the terminal were ventricular fibrillation and 6 of 27 events aboard aircraft were ventricular fibrillation. Defibrillators are only effective for ventricular fibrillation. Four victims were resuscitated and survived in the terminal group and two were resuscitated and survived in the aircraft group. If this data was extrapolated to the United States, then defibrillators aboard aircraft with trained responders would save about 10-20 lives per year. If defibrillators were placed in all terminals with trained responders, an additional 60-80 lives might be saved. The high incidence of ventricular fibrillation in the terminals is probably due to the fact that most of these events are witnessed. The victim is standing or running and suddenly collapses which is immediately noticed. On aircraft, the patient is sitting in their seat and does not fall or visibly collapse. Most observers feel that the victim has gone asleep. It is only when the victim does not wake up for breakfast on long international flights or does not get up when the plane reaches the gate that the event is recognized. This explains the reported high incidence of aircraft cardiac arrests upon plane arrival at the gate. The other high risk periods appear to be in the terminal and just after boarding when the victim is under the highest stress. Even though the incidence of events is very low, it is interesting to note that the event rate is 20 times what would be expected from the same aged individuals doing their normal daily activity; this points out that air travel is associated with stress. Many of the victims have terminal illnesses or are elderly.

The issue of placing defibrillators on airplanes and in terminals has only been partially addressed by several major organizations. The American College of Emergency Physicians and the American College of Cardiology do not have an official position on placing defibrillators on airplanes. The position of both organizations has been to encourage methods that can improve survival from

cardiac arrest. Both organizations feel that any proposed strategy should be evaluated for the benefit to risk ratio and have an acceptable cost-benefit analysis. The American Heart Association has stated that first responder defibrillation should be utilized in many venues and includes aircraft and terminals in those venues. Clearly, defibrillators on aircraft and in terminals would improve survival for some individuals. The cost-benefit analysis aboard aircraft is unique. If a system such as the one Qantas Airlines uses is utilized, then the reduction in aircraft diversions saves more money than the equipment and training costs; therefore such a program is potentially profitable for the airlines at the same time it provides a service. According to Qantas, the passengers and families are very appreciative of the effort even when it is unsuccessful. The only negative reported by Qantas is the stress on the crew members when they were unsuccessful; this is a common problem with emergency personnel and healthcare providers. The only question is the benefit to risk ratio. Newer types of defibrillators have markedly reduced the risk of defibrillation aboard an aircraft, as the electrodes are pasted to the patients chest, making it less likely for high voltage to be delivered to a rescuer, passenger, or to the metal frame of the aircraft. On smaller aircraft, there may be a problem with space. To perform CPR a patient, the victim must be lying on their back in a position where the rescuers can compress the chest and ventilate (breathe) the patient. To defibrillate the patient, the victim cannot be touching another person or metal. Some aircraft may be too small to provide adequate room for treatment. To perform CPR and defibrillate the patient, at least two and possibly three aircraft personnel are needed. It would be best to have at least four crew members available. One to perform chest compressions, one to ventilate the patient, one to defibrillate the patient, and the fourth to handle other problems and communication. This could possibly be reduced to two individuals; however, this will take further training and evaluation.

Based upon present information, in my professional opinion, it makes sense to place defibrillators in terminals and on wide body aircraft, particularly those with long flights and who carry older individuals. These have a higher incidence, there is sufficient room, and there is an adequate number of crew members. Placing defibillators on smaller aircraft must be evaluated carefully. Smaller jets that have at least three cabin personnel probably have enough space and personnel to do the job safely and effectively. We need to evaluate smaller aircraft and those with only two cabin personnel. With present technology, aircraft with no or one cabin attendant should probably not be equipped with defibrillators. This is a technology that has benefit properly applied. Further research and evaluation is needed to improve the results obtained in limited studies.

Implantable Defibrillators and Amiodarone

Recently the AVID study was reported verbally at the NASPE meeting. This study randomized patients to an implantable defibrillator or amiodarone . At one, two and three years the AICD (defibrillator) group had 38%, 26%, and 30% fewer deaths respectively. The one confounding problem was that 42% of the AICD group received beta blocking agents as compared to only 17% of the amiodarone treated group. Thus, it appears that an AICD + beta blockade is better than amiodarone.

Conclusions

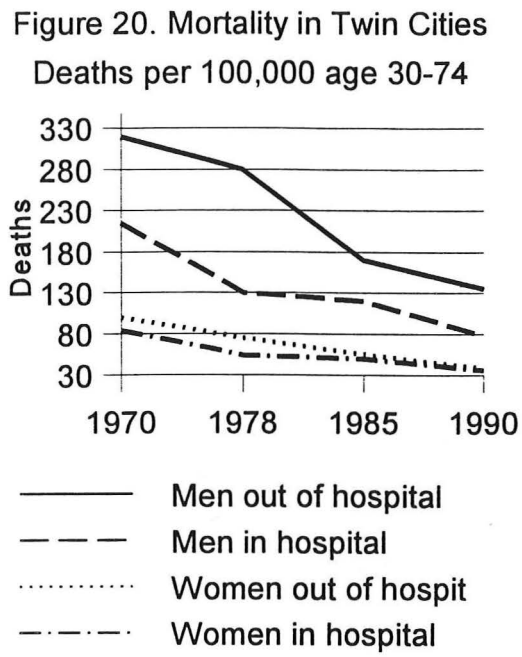

Figure 20 McGovern PG et al: N Engl J Med 334:884. 1996

The geographic variation in the incidence of sudden cardiac death is predominantly due to variations in the incidence of coronary heart disease. The reason for the geographic variations appears to be due mostly to variations in risk factors for coronary heart disease. The decline in the incidence of sudden cardiac death is predominantly due to the decline in the incidence of coronary heart disease. Figure 20 shows that in men and women the decline in out-of-hospital and in-hospital deaths appear to parallel functions.[138] It is of interest that the out-of-hospital mortality declined from 1970 to 1988, a time when the use of anti-arrhythmic agents was increasing rapidly. In 1988 the CAST trial caused a marked reduction in the use of anti-arrhythmic agents. The use and discontinuation of anti-arrhythmic agents appear not to have had an effect on mortality. Sudden cardiac death has declined due to alterations in risk factors. The best way to continue the reduction in the incidence sudden cardiac death is to continue to treat the underlying disease process. Use of agents that can prolong life by interacting with the disease process will have the greatest reward. The use of implantable defibrillators, possibly amiodarone, and catheter ablation of the arrhythmias remain the only ways of treating the arrhythmia and possibly prolonging life.

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