Prevention of sudden cardiac death in the community

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Pathological aspects of sudden death in the Mediterranean area

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Sudden cardiac death (SCD) is the most important challenge of modern cardiology. As in present times it can be prevented and the knowledge of pathological mechanisms as well as the correlation between SCD and associated diseases and risk factors is crucial. There is a great geographical variety in the incidence of SCD and ischemic heart disease (IHD) as its main underlying cause with lower incidence of IHD and SCD episodes in Mediterranean countries. However, although the incidence of SCD in Spain is one of the lowest in the industrialized countries, a recently published study has demonstrated that the incidence of atherosclerotic plaques in young people detected at autopsy is unexpectedly high. The pilot study of the EULALIA Trial, based on necropsy studies of SCD victims in Catalonia, demonstrated differences between the Mediterranean region and Anglo-Saxon countries. A lower incidence of associated IHD (50 vs 80-90%), a lower incidence of acute coronary syndromes in ischemic patients (33 vs 50%) and a higher incidence of left ventricular hypertrophy (64 vs 43%) was found in SCD victims from the EULALIA Trial. The relationship between smoking and coronary thrombosis has been confirmed.

Cardiovascular diseases cause more than 16 millions of deaths a year and in the industrialized countries are responsible for about 40% of total mortality. Sudden death represents 10-30% of total mortality, and about 50% of deaths in patients with cardiovascular diseases[1,2]. Sudden cardiac death (SCD) is responsible for about 90% of all sudden deaths. It has also been demonstrated that in Anglo-Saxon countries ischemic heart disease (IHD) is the underlying cause of about 80-90% of SCD[2]. On the other hand SCD is very often a first manifestation of IHD[2,3].

SCD is the most important challenge of modern cardiology. The importance of this problem is stressed by the fact that SCD from definition may occur suddenly in individuals that in spite of their heart disease are able to live a normal or near normal life[3,4]. Nowadays SCD can be prevented with the implantation of modern cardioverter-defibrillator devices; however in many cases it is difficult to determine a group of patients who in the highest degree may benefit from this therapy. The knowledge of pathological mechanisms as well as the correlation between SCD and associated diseases and risk factors is based mainly on the studies from Anglo-Saxon countries. In a study of Burke et al.[5] assessing the coronary risk factors and plaque morphology in 113 men with coronary artery disease who died suddenly, elevated cholesterol serum concentrations predisposed patients to rupture of vulnerable plaques, whereas cigarette smoking predisposed to acute thrombosis. Pathological findings revealed acute coronary thrombosis in 52% of SCD victims, while in the resting 48% severe narrowing of coronary arteries with atherosclerotic plaque without thrombosis (stable plaque) were found. A population-based study in the Maastricht area analyzing the incidence and clinical characteristics of out-of-hospital sudden cardiac arrest showed that sudden cardiac arrest is very often the first manifestation of heart disease (53% of women and 44% of men), thus the majority of victims cannot be identified before the event[6].

The incidence of SCD in adults according to the World Health Organization ranges from 19 to 159 cases/100 000/year in men and from 2-35 cases/100 000/year in women[1].

However, there is a great geographical variety in the incidence of SCD and IHD. Mortality due to IHD varies from 50-120/100 000/year in Japan and Mediterranean countries to up to 600/100 000/year in Russia and other economies in transition countries[7]. Similarly to the low incidence of acute coronary syndromes (ACS) there is a significantly lower incidence of SCD episodes in Mediterranean countries. The incidence of SCD in Spain is estimated at about 9000 cases a year in patients between 25 and 74 years and is one of the lowest in the industrialized countries[8]. Simultaneously, and in spite of the high incidence of stable plaques in young people the incidence of acute myocardial infarction observed in Spain is low (MONICA study)[9].

A low incidence of ACS in the Mediterranean region may probably be explained by the effect of diet, and in a broad aspect related with the "Mediterranean culture" and other factors as genetics[10]. Regarding risk factors, in Spain comparing to Anglo-Saxon countries a lower incidence of acute myocardial infarction was observed at the same serum levels of total cholesterol[11]. However, as we have already stressed, a recently published study has demonstrated that in spite of a low incidence of ACS and SCD episodes in Spain the incidence of atherosclerotic plaques in young persons detected at autopsy is unexpectedly high. Therefore, it is probable that in Spain atherosclerosis evolves more slowly and that some environmental factors prevent coronary plaques from becoming unstable[12].

Nevertheless, little is known about the underlying factors determining the geographical differences in IHD and SCD incidence between Mediterranean and Anglo-Saxon countries. Therefore with the aim to know: a) how many SCD are associated with IHD, b) how many SCD are due to ACS; c) what is the relationship between risk factors and SCD, and finally d) what pathological alterations can be found in SCD victims, we decided to realize a project called MUSA (Muerte Subita en Adulto: Sudden Death in Adults). This study contains two arms: the EULALIA Trial which is the pathological study of SCD victims, and the MUSIC 2 (Muerte Subita en Insuficiencia Cardiaca) which focuses on SCD in patients with heart failure.

The pilot study of the EULALIA Trial was performed between January 2002 and January 2003 and was based on the necropsy studies of SCD victims in Catalonia. The study included 50 victims (41 men, 9 women, mean age 54 years) of out-hospital sudden death with the autopsy performed within the first 18 hours *post-mortem*. The aim of this project was to determine the relationship of SCD to different epidemiological, clinical and biochemical parameters as well as to determine the percentage of ACS, atherosclerotic plaques, and to classify the plaques.

Pathological signs of coronary artery disease were found in 25 cases (50%) in the EULALIA Trial: in this 36% presented with ACS and 64% without ACS. Detailed data regarding the underlying heart disease and the morphology of the atherosclerotic plaques found at autopsy are displayed in figures 1 and 2. Comparing morphological characteristics of atherosclerotic plaques with a study of Burke et al.[5] we found a lower incidence of acute coronary thrombosis (36 vs 52%) as well as a lower incidence of ruptured plaques (44 vs 69%) in case of ACS. The correlation between smoking and acute thrombosis

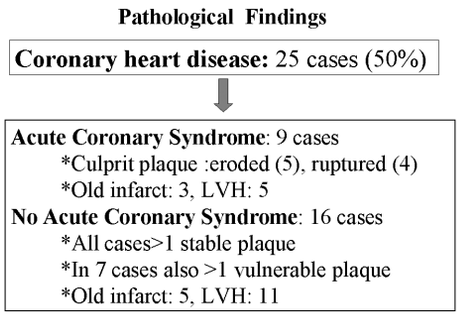

Figure 1. *Pathological findings in sudden cardiac death victims with coronary artery disease detected at autopsy. LVH = left ventricular hypertrophy.*

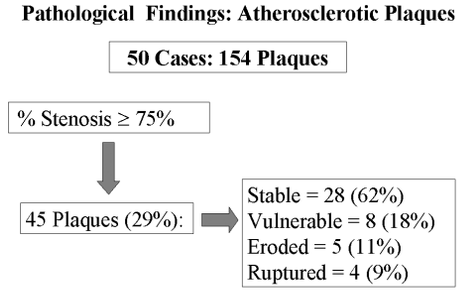

Figure 2. *Characteristics of the atherosclerotic plaques found at autopsy of sudden cardiac death victims from the EULALIA Trial pilot study.*

Table I. Pathological findings at autopsy in 50 victims of sudden cardiac death in the EULALIA Trial pilot study.

Underlying heart disease	No. cases
Coronary artery disease	25
Acute coronary syndrome	9
Stable coronary artery disease	16
No coronary artery disease	25
Cardiovascular disease	20
Left ventricular hypertrophy	5
Dilated cardiomyopathy	3
Hypertrophic cardiomyopathy	1
Amyloidosis	1
Valvular heart disease	2
Atrial septal defect	1
Pulmonary embolism	2
Aortic dissection	1
Toxics	
Alcohol	3
Cocaine	1
No cardiovascular disease	3
No associated disease	2

was confirmed. In the remaining 25 of cases of SCD victims with no coronary artery disease at autopsy there were 20 cases with other underlying cardiovascular diseases (as left ventricular hypertrophy, dilated cardiomyopathy, hypertrophic cardiomyopathy, etc.). Three deaths were not related to any cardiovascular disease and in 2 cases no associated disease was found (Table I).

Therefore the EULALIA project has demonstrated differences between the Mediterranean region and Anglo-Saxon countries regarding symptoms preceding SCD (a higher incidence of patients with no prodromal symptoms or with dyspnea, a lower incidence of patients presenting with anginal pain) and coronary risk factors (a lower incidence of hypertension and dyslipidemia). We also found a lower incidence of associated IHD (50 vs 80-90%), a lower incidence of ACS in ischemic patients (36 vs 50%) and a higher incidence of left ventricular hypertrophy (64 vs 43%).

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DOES INTERVENTION BY LAY PERSONNEL IMPROVE THE SURVIVAL AT DISCHARGE OF OUT-OF-HOSPITAL CARDIAC ARREST VICTIMS?

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Introduction

Immediate defibrillation is the single most effective therapy to reverse ventricular fibrillation and cardiac arrest. Conditions for defibrillation are often optimal for only as little as 3 min after the onset of arrhythmia so any delays can be critical. Public access defibrillation with lay personnel trained to use automated external defibrillators (AEDs) has been introduced to minimize the delay before delivery of a countershock outside hospital. The use of AEDs by persons other than paramedics and emergency medical technicians is advocated by the American Heart Association and other scientific organizations. Recent data on the outcomes when the devices are used by non-medical personnel for out-of-hospital cardiac arrest are encouraging.

Background

The once physician-only skill of defibrillation has nowadays become a simple non-medical procedure. Thanks to the effort of medical manufacturers lay personnel, both trained and untrained, is emerging as the next level of emergency care responders able to use a defibrillator. AEDs are simplified defibrillators that can be used by non-health care professionals. The operator places two electrode pads on the chest of a collapsed person. The AED then determines whether or not the person has a ventricular arrhythmia requiring defibrillation. The machine gives the operator voice instructions to either shock the patient by pressing a button, or to initiate cardiopulmonary resuscitation. Today, airports, airlines, casinos, cruise ships, and other public venues have modernized their first aid kits to include an AED.

Lay responders and survival

Early schemes to provide defibrillators in public places with lay volunteers trained to their use have reported favorable results.

In the first year after their introduction at O'Hare airport (Chicago, IL, USA)[1], several airline passengers who had a cardiac arrest were successfully resuscitated after defibrillation by staff at the airport. Defibrillators were installed at 60 to 90 s walk apart throughout passenger terminals. The use of defibrillators was promoted by public-service videos in waiting areas, pamphlets, and reports in the media. Over a 2-year period, 21 persons had non-traumatic cardiac arrest, 18 of whom had ventricular fibrillation. With two exceptions, defibrillator operators were good Samaritans, acting voluntarily. Eleven patients with ventricular fibrillation were successfully resuscitated. The rescuers of 6 of the 11 successfully resuscitated patients had no training or experience in the use of automated defibrillators, although 3 had medical degrees. Ten of the 18 patients with ventricular fibrillation were alive and neurologically intact at 1 year. Chicago airport experience is very important because it demonstrates how simple is the use of AEDs: most of the users had no duty to act and no prior training in the use of these devices.

In Las Vegas[2], security staff at casinos resuscitated 105 patients in ventricular fibrillation, 56 (53%) of whom survived to be discharged from hospital. The locations where the defibrillators were stored in the casinos were chosen to make possible a target interval of ≤ 3 min from collapse to the first defibrillation. The closed circuit television surveillance at the casinos enabled rapid identification of potential patients, and 74% of those defibrillated within 3 min of collapsing survived.

Other locations where trained lay people undertake defibrillation are in aircraft and ships, when a conventional response from the emergency services is impossible. In one report, the cabin crew of US airlines[3] successfully defibrillated all patients with ventricular fibrillation, and 40% survived to leave hospital.

In the United Kingdom[4], the remoteness of rural communities often prevents the ambulance service from responding quickly enough to a cardiac arrest or to the early stages of acute myocardial infarction. Increasingly, trained lay people (termed first responders) living locally and equipped with an AED are dispatched by ambulance control at the same time as the ambulance. They are able to reach the patient and provide initial treatment, including defibrillation if necessary, before the ambulance arrives.

Other strategies used to decrease response times include equipping the police and fire services with AEDs. This is the case of the "Piacenza Progetto Vita"[5] where policemen were trained to use AEDs with a brief training course of defibrillation without cardiopulmonary resuscitation instruction. Overall survival was 5.6% (11/197): survival improved from 2.9% (4/134) with EMS intervention to 11.1% (7/63) when the "Progetto Vita" was activated ($p < 0.05$). Survival rate on "shockable" rhythm was significantly higher in lay volunteers group than EMS (43.7% in group treated by volunteers vs 16.6% in those treated by EMS aid).

To further support the beneficial effect on survival of early defibrillation in the community is the data of the prospective cohort study conducted in Olmstead County[6] (MN, USA). All patients who had an out-of-hospital cardiac arrest from November 1990 to December 2000 after implementation of a local early defibrillation program were followed to determine long-term survival and quality of life. Of the 200 patients with an out-of-hospital cardiac arrest with ventricular fibrillation, 145 (72%) survived to hospital admission with spontaneous circulation, 84 (42%) survived to hospital discharge, and 79 (40%) were neurologically intact at discharge. Long-term survival was realized by 60 patients (30%). For analysis, patients with significant neurological impairment at discharge were considered non-survivors. The mean length of follow-up was 4.8 ± 3.0 years. The expected 5-year survival rate (79%) was identical to that among age-, sex- and disease-matched subjects. Long-term survival and quality of life of patients resuscitated from a cardiac arrest has been demonstrated to be similar to that of control subjects.

Most studies of cardiac arrest have used return of spontaneous circulation and survival to hospital discharge as primary endpoints. The study by Bunch et al.[6] shows that long-term survival is also possible and that those who survive report a good quality of life.

In contrast, patients with ventricular fibrillation in the Ontario Prehospital Advanced Life Support study[7] had a rate of survival to hospital discharge of only 10%. This much larger study included 3447 patients with out-of-hospital ventricular arrhythmia. The authors concluded that shorter times to defibrillation are crucial to reduce the rate of death from ventricular fibrillation.

We are waiting for the results of the PAD Trial[8] the first prospective, multicenter, randomized clinical study testing whether volunteer, non-medical responders can improve survival from out-of-hospital cardiac arrest by using AEDs. The study has been conducted at 24 centers in the United States and Canada for 15 months. Approximately 1000 community units (e.g. apartment or office buildings, gated communities, sports facilities, senior centers, shopping malls, etc.) were randomized to treatment by trained lay persons who will provide either cardiopulmonary resuscitation alone or cardiopulmonary resuscitation plus the use of an AED, while awaiting arrival of the community emergency medical service responders. The primary endpoint is the number of out-of-hospital cardiac arrest victims who survive to hospital discharge. Secondary endpoints include neurological status, health-related quality of life, costs, and cost-effectiveness. This study will better clarify the effects on survival of public access defibrillation.

Conclusion

Lay persons equipped with AEDs (including policemen) are saving the lives of many sudden cardiac arrest victims in a variety of settings so increasing public safety. Broadening access to and training in AED use beyond health care professionals can help to reduce the time to defibrillation and therefore increase survival from cardiac arrest. Deciding who to be trained in AED use (e.g., police officers, security guards, general public), where to place AEDs (e.g., shopping malls, arenas, airports) and how to fund early defibrillation programs will help to determine the success of these programs. Meanwhile lay people (often staff working in public places) who are trained to use automated defibrillators must operate within a system that is under medical control but respond independently, usually on their own initiative, when someone collapses. A minimal training (training of few hours or video self-instruction) is needed for AED safely use.

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IN-HOUSE AUTOMATED EXTERNAL DEFIBRILLATORS FOR HIGH-RISK PATIENTS: RATIONALE AND PERSPECTIVES

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Automated external defibrillators and sudden cardiac death

Sudden cardiac death is the single most important cause of death in the adult population of the industrialized world. The incidence of out-of-hospital sudden cardiac death varies with age, gender and presence or absence of a history of cardiovascular disease[1].

The drive for a widespread use of automated external defibrillators (AEDs) in unconventional (i.e. out of hospital) sites was directly elicited by the clinical evidences showing that ventricular fibrillation or ventricular tachycardia are the most commonly encountered rhythms when first responders arrive early at the scene of cardiac arrest[2,3] and by the fact that early defibrillation is significantly associated with higher rates of survival in the clinical setting[4].

Subgroups of patients with coronary disease are at higher risk of sudden death and they are identifiable on the basis of their clinical profile including previous myocardial infarction, ischemia, impaired left ventricular function, and ventricular tachyarrhythmias. Diagnostic examinations, drugs, devices and procedures are available for the identification and treatment of these patients so that their risk of sudden cardiac death can be reduced. However these subgroups of individuals at greater risk of sudden death include only a relatively small proportion of the total number of sudden death victims in the population.

Most studies support the concept that the largest proportion of sudden cardiac deaths occur as first manifestation of cardiac disease and therefore preventive strategies based on risk stratification will never be able to effectively reduce this share of sudden cardiac deaths. Therefore the best hope for victims of sudden cardiac death in the absence of previously recognized cardiac risk, lies in either very rapid response from ambulances or from community use of AEDs. Experience of recent years has shown that acceptable results from defibrillation can be achieved only if a shock can be administered within 4-5 min of collapse, with slight extension of this window achieved by cardiopulmonary resuscitation especially if it is administered immediately before the shock.

Strategies for community defibrillation with automated external defibrillators

The two main strategies for early defibrillation in the community are a) the establishment of faster dispatched responses by ambulance services or unconventional first responders (police, fire fighters, etc.), and b) on-site AEDs deployment in critical places that are likely to have cardiac arrests within the area from time to time. The latter will achieve better success rates per use of defibrillator than general community schemes but more AEDs need to be deployed. It has been suggested[5] that one use

every 5 years might be considered cost-effective for the second type of deployment but sites can be identified with cardiac arrest incidence appreciably higher than this figure.

General concepts on the use of automated external defibrillators

AEDs have been first tested in two-tired rescue systems in Cook County and Seattle (WA, USA) by Eisenberg et al.[6] and Weaver et al.[7]. These experiences formed the basis for a quick and widespread use in similarly formed emergency medical services worldwide.

Since then, early defibrillation with AEDs has been evaluated in a number of different environmental settings, spanning from hospitals, airplanes, casinos to local urban communities and with different typology of "shock deliverers" including non-trained or minimally trained subjects (fire-fighters, flight attendances, police officers and security guards). Most of such trials provided evidences for efficacy and recently a large scale study has added one important information on long-term outcome and quality of life of individuals resuscitated from cardiac arrest demonstrating that after discharge from hospital, cardiac arrest survivors have both survival and quality of life similar to that of an age-matched population[8].

Home use of automated external defibrillators

Among the major findings of the Maastricht study[9], that monitored all cases of out-of-hospital cardiac arrest occurring in victims between 20 and 75 years of age, an overall yearly incidence of sudden death of 1 per 1000 per year was recorded. Interestingly, 80% of out-of-hospital cases occurred at home and about 15% on the street or in a public place.

These data prompt the need for a careful assessment of the possible positive impact of AED deployment at the patient's home. However, this issue has been only poorly explored until now. Even in an environment of more widespread use of implantable defibrillators several categories of patients could potentially benefit from in-home AED, e.g. high-risk post-infarction patients, fulfilling the MADIT II criteria in the first weeks after discharge[10], dilated cardiomyopathy patients and patients/families with inherited arrhythmogenic diseases.

Initial experiences with home use of AEDs in small groups of patients showed no benefit[11], while more recently Snyder et al.[12] carried out a telephone survey of businesses (n = 2678) and homes (n = 153) owning an AED that provided more encouraging data. Businesses reported that 209 (13%) had used an AED at least once, with 232 cases of known outcome. Of the 8 patients treated by AED shocks, 6 patients (75%) survived. These data support the concept that AED deployment at home or offices may save lives, but further confirmations are still needed to prove or dismiss this hypothesis.

Conclusions

A large amount of clinical evidence shows that early defibrillation saves lives. When AEDs are used by unconventional responders (fire fighters or police) or when they are deployed in mass gathering places, there is a clear survival benefit. The rationale for extending the use of AEDs to private places is based on the evidence that the majority of sudden cardiac deaths occur at home. Despite at present the experience with the home use of AEDs is still limited and there is a strong need for controlled trials evaluating this strategy, the available evidences are encouraging.

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