Clinical Characteristics of Unexplained Sudden Cardiac Death in Korea

Jeong Gwan Cho, MD*; Hyung Wook Park, MD; Jay Young Rhew, MD; Sang Rok Lee, MD; Woo Kon Chung, MD; Ok Young Park, MD; Weon Kim, MD; Kye Hun Kim, MD; Kyung Tae Kang, MD; Sang Hyun Lee, MD; Nam Ho Kim, MD; Jong Cheol Park, MD; Young Keun Ahn, MD; Myung Ho Jeong, MD*; Jong Chun Park, MD*; Jung Chaee Kang, MD*

In Western countries, sudden cardiac death (SCD) is closely related to coronary artery disease, but in Korea the clinical characteristics of SCD are not well determined. Over a 4-year period (June 1995 to May 1999), 186 cases of SCD, ranging in age from 16 to 75 years, were admitted to the Chonnam National University Hospital. In 82 (44.1%) of these, neither symptoms nor evidence of structural heart disease was found and so their clinical characteristics were investigated. There were 66 (80.5%) men and 16 (19.5%) women (male/female ratio = 4.1:1). The mean age was 50±14 years: 19 (23.2%) were in their 40s, 21 (25.6%) in their 50s, and 17 (20.7%) in their 60s. The time of circulatory collapse witnessed in 68 cases of SCD showed 2 peaks: between midnight and 03.00h (n=16, 23.5%) and between 09.00h and midday (n=15, 21.2%). Unexplained SCD occurred at home in 48 (64.9%) cases and on the street in 12 (16.2%); it occurred during normal daily routine activity in 23 (39.6%) and during sleep in 15 (25.9%). Thirty-three patients (40.2%) experienced various prodromal symptoms, including chest discomfort (n=13, 15.9%) and dyspnea (n=8, 9.8%). The electrocardiogram taken on arrival recorded asystole in 65 (79.3%) and ventricular fibrillation in 17 (20.7%). Idiopathic ventricular fibrillation was diagnosed in 14 (10 men, 4 women; 45±11 years) of 21 patients who recovered spontaneous circulation. Five (6.1%) patients were discharged alive, and an implantable cardioverter-defibrillator was implanted in 2. Unexplained SCD is common in Korea and develops predominantly in middle-aged males around midnight or in the late morning usually with no prodromal symptoms (59.8%). Idiopathic ventricular fibrillation is thought to be one of the important causes. (Jpn Circ J 2001; 65: 18–22)

Key Words: Idiopathic ventricular fibrillation; Unexplained sudden cardiac death

Sudden cardiac death (SCD) is defined as unexpected natural death because of circulatory collapse within 1 h of the onset of acute symptoms in a person who leads an uneventful life.1–2 SCD has a high mortality rate; even in Seattle, USA where the emergency medical care system is so well equipped that the emergency medical service arrives and performs cardiopulmonary resuscitation and defibrillation within 5 min, less than 10% of SCD patients are successfully resuscitated and discharged alive without neurological complications.3 In Western countries, including the USA, coronary artery disease (CAD) is reported to be related to approximately 80% of SCD cases and so is the most common underlying cause.4 In the Framingham Study, a 26-year survey of 5,128 subjects (aged 30–62 years) without evidence of cardiac disease at entry, SCD accounted for 13% of all natural deaths and 50% of the mortality from CAD.5–7

It is well documented that SCD is usually caused by ventricular tachyarrhythmias, but the cardiac rhythms of SCD victims differ with the time elapsed from the onset of circulatory collapse. Ventricular fibrillation (VF) is recorded in approximately 70%, and fast ventricular tachycardia, bradyarrhythmias, or asystole in the remaining cases.8–10

In Korea, the incidence of SCD is increasing with the rapid increase in CAD observed over the past 10 years, and has recently emerged as an important national health problem. However, the clinical characteristics and underlying diseases of SCD are not yet well determined in this country. In a report of the 51-year experience of autopsies conducted between 1946 and 1996 at the Korea National Institute of Scientific Investigation, 10% of deaths were intrinsic sudden death.11 That study documented the underlying disease as cardiovascular disease in 49.7%, central nervous system disease in 13.6%, and pulmonary disease in 13.9%, and suggested that CAD played a less important role in SCD in Korea than in the West.

The present study aimed to clarify the clinical characteristics and mechanism of SCD in Korea so that it can be managed successfully.

Methods

From June 1995 to May 1999, 186 cases of SCD were admitted to the Chonnam National University Hospital in Kwangju, Korea. The hospital records were reviewed and the patient’s relatives were interviewed in person or by telephone. Of these, 104 patients (55.9%, 67 male, mean age 61±9 years) had an underlying disease, which was hyperten-
Unexplained Sudden Cardiac Death in Korea

Table 1 Age and Sex Distribution of 82 Patients With Unexplained Sudden Cardiac Death

<table>
<thead>
<tr>
<th>Age group</th>
<th>10s</th>
<th>20s</th>
<th>30s</th>
<th>40s</th>
<th>50s</th>
<th>60s</th>
<th>70s</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>1</td>
<td>5</td>
<td>9</td>
<td>17</td>
<td>18</td>
<td>12</td>
<td>4</td>
<td>66 (80.5)</td>
</tr>
<tr>
<td>Female</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td>3</td>
<td>16 (19.5)</td>
</tr>
<tr>
<td>Total (%)</td>
<td>1 (1.2)</td>
<td>7 (8.5)</td>
<td>10 (12.2)</td>
<td>19 (23.2)</td>
<td>21 (25.6)</td>
<td>17 (20.7)</td>
<td>7 (8.5)</td>
<td>82 (100)</td>
</tr>
</tbody>
</table>

Fig 1. Distribution of the time of onset of unexplained sudden cardiac death.

Fig 2. Time of onset of sudden cardiac death caused by idiopathic ventricular fibrillation.

Results

Of the 82 cases of unexplained SCD, 66 (80.5%) were men and 16 (19.5%) women (male/female ratio = 4.1:1), and their mean age was 50±14 years (Table 1). The most prevalent age group was the 50-year-olds (25.6%), followed by the 40- (23.2%) and 60-year-olds (20.7%).

Unexplained SCD (n=68) developed between midnight and 03.00 h in 16 (23.5%), between 03.00 h and 06.00 h in 6 (8.8%), between 06.00 h and 09.00 h in 10 (12.2%), between 09.00 h and midday in 15 (22%), between midday and 15.00 h in 8 (11.8%), between 15.00 h and 18.00 h in 6 (8.8%), between 18.00 h and 21.00 h in 5 (7.4%), and between 21.00 h and midnight in 2 (2.9%) (Fig 1).

The attack (n=74) occurred in the home in 48 (64.9%) patients, the street in 12 (16.2%), in a liquor bar in 2 (2.7%), in a bathing house in 3 (4.1%), in an inn in 3 (4.1%), in a car in 3 (4.1%), and in a public building including a hospital in 3 (4.1%). The activity at the time of circulatory collapse (n=58) was routine daily activity in 23 (39.6%) patients,
sleep in 15 (25.9%), resting in 9 (15.5%), exercising in 4 (6.9%), drinking alcohol in 4 (6.9%), bathing in 2 (3.4%), and defecation in 1 (1.7%).

Forty-nine (59.8%) patients did not experience any discomfort before SCD, but 33 (40.2%) experienced prodromal symptoms, including chest pain (n=13, 15.9%), palpitations (n=8, 9.8%), dyspnea (n=8, 9.8%), dizziness (n=2, 2.4%), headache (n=1, 1.2%), and epigastric discomfort (n=1, 1.2%).

The electrocardiogram (ECG) on arrival at the hospital documented ventricular asystole in 65 patients (79.3%) and VF in 17 (20.7%). The time from the onset of circulatory collapse to the ECG recording was significantly shorter in the patients with VF than in those with asystole (15±2 vs 18±60 min, p<0.001) and VF was recorded significantly more frequently in the patients who were discharged alive (n=5) than in those who died (n=77) during hospitalization (80.0% vs 18.2%, p<0.01). The time interval from circulatory collapse to arrival at the hospital was significantly shorter in the patients who were discharged alive than in those who died in the hospital (13±3 vs 90±126 min, p<0.001).

Twenty-one patients (25.6%) recovered spontaneous circulation, allowing an extensive diagnostic examination. ECG, laboratory tests, and echocardiography were performed in all these patients and cardiac catheterization and an electrophysiology study in 4. Echocardiography revealed no abnormality in 14, mild regional wall motion abnormality in 2, and mild valvular regurgitation in 5. Fourteen of the 21 patients were diagnosed as idiopathic VF (10 men, 4 women; 45±11 years), which accounted for 7.7% of all SCD cases and 17.1% of unexplained SCD.

The time of SCD attack because of idiopathic VF was between midnight and 03.00 h in 5 (35.7%) patients, between 03.00 h and 06.00 h in 2 (14.3%), between 06.00h and 09.00 h in 2 (14.3%), between 09.00 h and midday in 1 (7.1%), between midday and 15.00 h in 2 (14.3%), and between 15.00h and 18.00 h in 2 (14.3%) (Fig 2), showing that attacks were most frequent in the 3 h after midnight. SCD caused by idiopathic VF developed at home in 6 (42.9%), in a street in 6 (42.9%), in a car in 1 (7.1%), and in a liquor bar in 1 (7.1%). It developed during daily routine activity in 7 (50.0%), during sleep in 4 (28.6%), during rest in 2 (14.3%), and during defecation in 1 (7.1%). Seven patients (50.0%) experienced prodromal symptoms, such as chest pain (n=3), dyspnea (n=2), and palpitations (n=2). The ECG after restoration of sinus rhythm documented incomplete right bundle branch block (RBBB) in 2, sinus bradycardia in 2, and mild QT prolongation in 1. Echocardiography demonstrated no abnormality except a relaxation abnormality in 5 patients. Late potential was recorded in 3 of 4 patients who underwent a signal-averaged ECG. In the 4 patients who underwent an electrophysiologic study, VF was reproducibly induced by programmed electrical stimulation in 3. None of the 4 patients undergoing coronary angiography had significant stenosis or abnormal ventricular wall motion. Four idiopathic VF patients were discharged alive, accounting for the majority (80%) of the 5 patients who were discharged alive. Of the 5 surviving patients discharged alive, amiodarone was prescribed in 3 and a cardioverter-defibrillator was implanted in 2.

**Discussion**

The present study examined the clinical characteristics of SCD, which has recently become a major public health problem in Korea, where the prevalence of CAD is increasing sharply, although it is still low compared with Western countries. We found that 44.1% of SCD cases were patients with no structural heart disease, and that unexplained SCD commonly occurred in middle-aged men, around midnight and in the late morning, at home, during daily routine activities. Approximately 60% of the cases of unexplained SCD had no prodromal symptoms and idiopathic VF caused 17% of the cases.

Approximately 300,000–400,000 annual cases of SCD occur in the United States. Although CAD is known as the most common underlying disease, the cause of SCD cannot be determined exactly in many cases. Raymond et al who investigated the cause of out-of-hospital SCD in adults less than 45 years old showed that the cause of SCD differed with each age group.

Although epidemiologic and clinical characteristics are very important in managing SCD, such studies are very scarce in Korea. In 1984, Yoon reported the cause of death and underlying or associated disease in patients who had died within 24 h of the onset of symptoms and undergone a medicolegal autopsy to investigate the cause of death. He reported that the underlying or associated disease was CAD in 16.6%, heart failure in 12.2%, myocardial infarction in 5.2%, myocarditis in 2.9%, and undetermined in 13.6%. No structural heart disease was found in 95 (15.3%) of 613 cases who died within 1 h of the onset of symptoms. That incidence (15.3%) of unexplained SCD is lower than in the present study (44.1%) and may be because the 2 studies are separated by 16 years and Yoon’s study was based on medicolegal autopsy in contrast to our clinical study. In our study, acute or old myocardial infarction was only found in 23 (12.4%) of 186 SCD patients and SCD was unexplained despite extensive examination in 82 (44.1%), which are similar findings to those reported by Tokashiki et al in a study of the general population of Okinawa, Japan; they could not determine the cause of SCD in 53% of cases.

de Vreede Swagemakers et al studied the clinical characteristics and survival of out-of-hospital SCD (n=515) in The Netherlands between January 1991 and December 1994, and found that SCD was often the first manifestation of heart disease in 44% of men and 53% of women. In a study of SCD in northwest Greece, Goudevenos et al stated that SCD was the first manifestation of heart disease in 58% of 223 subjects who died suddenly.

Previous studies have demonstrated that the incidence of SCD increases with age, but SCD caused by CAD decreases. SCD occurs 3–4 times more often in men than in women confirmed by the present study in which SCD developed 4 times more often in men than in women.

It has been reported that SCD may be related to psychological stress and excessive exercise but Goudevenos et al found that 78% of SCD occurred in the resting state or during daily routine activity. We found that 93.1% of SCD occurred at rest or during daily activity. SCD has been reported to occur at home in 60–80% of cases, which is similar to our result of 64.9% of SCD cases occurring at home.

It is known that SCD has a circadian pattern. Goudevenos et al reported that SCD occurred most often between 09.00h and midday and Willrich et al reported that it occurred most frequently between 07.00h and 11.00h. The high incidence of SCD in the late morning has been explained by the increase in blood catecholamines, which provoke myocardial ischemia, arrhythmias, and hypercoag-
In our study, unexplained SCD occurred most frequently between midnight and 03:00 h, accounting for 23.5% of all SCD and is a similar circadian pattern to that seen in sudden unexplained death syndrome (SUDS), which occurs at night in young adults in South-East Asia and Japan\(^{23-28}\) and suggests that unexplained SCD in Korea is similar to SUDS rather than to SCD associated with CAD.

Weaver et al reported that VF was recorded on the ECG in 80% of patients with SCD\(^{29}\) and Hallstrom et al suggested that VF caused most SCD and degenerated into asystole with time\(^{30}\). In the present study, VF was recorded in only 17 (20.7%) patients whereas asystole was recorded in 65 (79.3%). The time interval from the onset of SCD to ECG recording was significantly shorter in the patients with VF than in those with asystole (15±2 vs 181±60 min, p<0.001) and the low incidence of VF in the present study is thought to be related to the delayed transport of the SCD victims to the hospital.

Idiopathic VF was diagnosed in 14 (10 men, 4 women; 45±11 years) of 21 patients who recovered spontaneous circulation with advanced life support. It accounted for 7.7% of all SCD cases, and 17.1% of unexplained SCD. It should be stressed that the role of idiopathic VF as a cause of SCD may have been underestimated, because complete diagnostic workup for underlying disease and idiopathic VF was impossible in the 61 patients who died without recovering circulation. Nevertheless, this study suggests that idiopathic VF may be one of the important causes of unexplained SCD in Korea.

Idiopathic VF is defined as VF in which neither underlying heart disease, including long QT syndrome and Wolff-Parkinson-White syndrome, nor electrolyte and metabolic disorders are documented, despite extensive investigation\(^{31}\). It has been reported that idiopathic VF accounts for 5–10% of patients resuscitated from out-of-hospital cardiac arrest,\(^{32-34}\) Idiopathic VF occurs in apparently healthy young adults\(^{35}\). In 1992, Brugada and Brugada described idiopathic VF characterized by a distinct ECG pattern of RBBB and right precordial ST elevation as Brugada syndrome,\(^{36}\) and recently, Chen et al\(^{37}\) demonstrated that this syndrome is related to a mutation in SCN5A, the cardiac sodium channel gene. In the current study, no case was diagnosed as Brugada syndrome, but it was suspected in a 43-year-old man who had a slightly dilated left ventricle on echocardiogram and slightly elevated cardiac enzymes. On the other hand, there is a report from the 1980s of young healthy South-East Asian refugees dying suddenly during sleep at night; the cause of death could not be determined, even autopsy. This was the first instance of SUDS and was regarded as an important cause of SCD in this population\(^{24,25}\). Nademanee et al\(^{37}\) observed ST elevation in precordial leads V\(_1\)-V\(_3\) on ECG in 59% (16/27) of SUDS patients in Thailand, and suggested that some of these patients might have Brugada syndrome. In the present study, incomplete RBBB was found in 2 patients, but no ST elevation typical of Brugada syndrome was seen. However, the unique ECG findings of Brugada syndrome are transient or concealed in some cases, in whom Class IA or IC sodium channel blockers, such as ajmaline, procainamide, and flecainide, may provoke RBBB and the characteristic ST elevation\(^{38}\). We did not perform such a provocation test and thus the possibility of Brugada syndrome in the patients diagnosed as idiopathic VF cannot be excluded completely.

In this study, we examined the clinical characteristics of SCD in Korea. Only 25% of the patients recovered spontaneouss circulation, so the diagnosis of underlying disease was usually based on interviews with relatives of the patients. Although there are some limitations, this study provides background information on the clinical characteristics of unexplained SCD in Korea.

References


33. Kudenchuk PJ, Cobb LA, Greene HL, Fahrenbruch CE, Sheehan FH: Late outcome of survivors of out-of-hospital cardiac arrest with left ventricular ejection fractions greater than or equal to 50% and without significant coronary arterial narrowing. *Am J Cardiol* 1991; 67: 704–708


