Risk of sudden cardiac death
Roxana Sadeghi(1), Nadia Adnani(2), Mohammad-Reza Sohrabi(3), Saeed Alipour Parsa(1)

Abstract

BACKGROUND: The aim of this study was to determine characteristics of patients with sudden cardiac arrest (SCA) and/or sudden cardiac death (SCD). We need an effective risk stratification method for SCD in patients without low left ventricular ejection fraction (LVEF).

METHODS: The study population of this cross-sectional study consisted of 241 patients with SCA or SCD who were admitted to an academic hospital, in Tehran, Iran, from 2011 through 2012. SCD was defined as unexpected death from cardiac causes, heralded by abrupt loss of consciousness within one hour of the onset of acute changes in cardiovascular status, or an unobserved death in which the patient was seen and known to be doing well within the previous 24 hours. Survivors of aborted SCD were also included in the study. Clinical and paraclinical characteristics as well as emergency department complications of patients were recorded.

RESULTS: The mean age of population was 66.0 ± 16.5 (17 to 90 years). Among the patients, 166 (68.9 %) were male, 50 (20.7%) were smoker, 77 (32.0%) had hypertension, 47 (19.5%) had diabetes mellitus, 21 (8.7%) had hyperlipidemia, and 32 (13.3%) had renal insufficiency. According to New York Health Association (NYHA) functional class, 31 (12.9%) patients were asymptomatic, 42 (17.4) and 99 (41.1%) subjects were in NYHA I and II, respectively and only 69 (28.6%) patients were in NYHA III or IV. In this study, presenting arrhythmia was pulseless electrical activity or asystole which was observed in 130 (53.9%) subjects. Ventricular tachycardia (VT) or ventricular fibrillation (VF) was seen in 53 (22%) patients. Cardiopulmonary resuscitation in emergency room was successful only in 46 (19.1%) subjects.

CONCLUSION: Low ejection fraction (EF) may be an independent predictor of sudden cardiac death in patients, but it is not enough. While implantable cardioverter defibrillators can save lives, we are lacking effective risk stratification and prevention methods for the majority of patients without low EF who will experience SCD.

Keywords: Death, Sudden Cardiac Arrest, Sudden Cardiac Death

Introduction
Cardiovascular disease is a leading cause of death in many parts of the world. Despite dramatic advances in diagnosing and treating cardiovascular disease, sudden cardiac death (SCD) still remains a major public health problem. Approximately one-half or more of all cardiac deaths are SCD and also, SCD can be the first manifestation.1

Few evidence is available in terms of incidence of sudden cardiac arrest (SCA) and/or sudden cardiac death (SCD) in Iran and in many countries.2,3 It is necessary to know the true magnitude of this problem for improving risk stratification and prevention methods. As death occurs shortly after the onset of symptoms, there is little time for treatment. Even in the presence of advanced systems for resuscitation of out-of-hospital cardiac arrest, the overall survival was reported in some studies as low as 4.6%.4 We rely on depressed left ventricular systolic function as the best predictor of SCD and mortality. But ejection fraction (EF) has a low sensitivity to predict SCD and the majority of patients who suffered from SCD have a preserved EF.5

Several factors have shown relationship with SCA/SCD like age, sex, smoking, type 2 diabetes

1- Assistant Professor, Cardiovascular Research Center AND Department of Cardiovascular Disease, Loghman Hakim Hospital, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2- Resident, School of Medicine, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3- Associate Professor, Department of Community Medicine, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Correspondence to: Roxana Sadeghi, Email: roxan.sadeghi@gmail.com
mellitus, systolic blood pressure, family history of coronary heart disease, family history of SCD, ischemic ST-changes during exercise test, abnormal myocardial perfusion imaging, coronary heart disease, low heart rate recovery, ventricular ectopy during recovery, increased QRS duration, abnormalities in QT interval and QT dispersion, abnormal signal-averaged electrocardiography (ECG), abnormal T-wave alternans, impaired heart rate variability, abnormal heart rate turbulence, low baroreceptor sensitivity, ventricular arrhythmias on Holter monitoring, low cardiorespiratory fitness, depression, and use of antidepressant drugs.6-8

To date, there is a lack of evidence with regards to SCD and it is required that pooled data is gathered, as such selection procedures will be performed more accurately, generating more reliable data. The implantable cardioverter defibrillator (ICDs) is very effective in treatment of patients at risk of SCA/SCD; however, the accuracy of available methods to predict SCD on an individual basis is limited.9

Materials and Methods

Study population
The study was a single-center, cross-sectional study and included two hundred forty one patients with SCA/SCD who have been admitted to an academic hospital, in Tehran, Iran, from July 1 2011 to July 1 2012. SCD was defined as unexpected, natural death from cardiac causes, heralded by abrupt loss of consciousness within 1 hour of the symptom onset, or an unobserved death in which the patient was seen and known to be doing well within the previous 24 hours. The location of SCA/SCD had to be in an out-of-hospital or emergency department setting. Survivors of aborted SCD were also included in the study. Subjects with known terminal illness (cancer), non-cardiac causes of sudden death (cerebrovascular accident, pulmonary embolism), traumatic, or overdoses related deaths were excluded. Family members were asked for permission to obtain information.

Two internal medicine physicians helped to obtain demographical, clinical, and paraclinical characteristics of selected patients which were recorded at the time of admission. Furthermore, family members reported symptoms of depression and antidepressant medication use were considered as a scale of measuring depression. When available, prior electrocardiograms, echocardiograms, and coronary angiograms were reviewed.

Statistical Analysis
Continuous variables were expressed as mean ± standard deviation, and dichotomous variables as frequencies. Statistical analysis was performed using SPSS version 16 (SPSS Inc., Chicago, IL, USA). Differences were examined using Student’s t-tests for continuous variables and chi-Square tests for dichotomous variables (or Fisher’s exact test as needed). A P < 0.05 was considered statistically significant.

Results
The mean age of study population was 66.0 ± 16.5 years (17 to 90 years). Among the patients, 166 (68.9%) were male, 50 (20.7%) were smoker, 29 (12%) were opium user, 10 (4.1%) were amphetamine user, no one was alcohol user, 77 (32.0%) had hypertension, 47 (19.5%) had diabetes mellitus, 21 (8.7%) had hyperlipidemia, 32 (13.3%) had renal insufficiency, and 4 (1.7%) had chronic lung disease.

Peripheral vascular disease was presented in 2 (0.8%) patients, cerebrovascular disease in 20 (8.3%), prior coronary artery disease in 48 (19.9%), prior congestive heart failure in 24 (10%), prior coronary artery bypass graft in 12 (5%), and prior percutaneous coronary intervention in 3 (1.2%) patients. The distribution of baseline characteristics of enrolled patients is shown in table 1.

Most of the patients were in low or moderate economical situation due to geographic place of the hospital, and 44% of patients had moderate or severe symptoms of depression. According to New York Health Association (NYHA) functional class, 31 (12.9%) patients were asymptomatic, 99 (41.1%) were in NYHA II class of symptoms, and only 69 (28.6%) patients were in NYHA III or IV classes. Clinical characteristics of selected patients are depicted in table 2.

Previous ECG was available in 149 (61.8%) patients with SCA/SCD. They showed normal findings in 25 (10.4%) patients, but pathological Q wave, left ventricular hypertrophia, left bundle branch block (LBBB), right bundle branch block (RBBB), and intraventricular conduction disturbance (IVCD) were observed in 119 (49.4%) patients. Previous echocardiograms were available in 115 (47.7%) subjects. The echocardiograms showed normal findings in 6 (2.5%) patients, and severe left ventricular systolic dysfunction was seen in 50 (20.7%) patients. Previous coronary artery angiograms were available in 32 (13.3%) patients and showed normal findings in 3 (1.2%) (Table 3).

In this study, presenting arrhythmia was pulseless electrical activity or asystole which was
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seen in 130 (53.9%) subjects. Ventricular tachycardia (VT) or ventricular fibrillation (VF) was observed in 53 (22%) patients. ECG findings of enrolled patients at admission are shown in Table 4.

Table 1. Baseline characteristics of enrolled patients with sudden cardiac arrest/sudden cardiac death

| Characteristics                  | n (%)          |
|----------------------------------|----------------|
| Total number                     | 241 (100)      |
| Males                            | 166 (68.9)     |
| Family history of CAD            | 26 (10.8)      |
| Family history of SCA/SCD        | 1.0 (0.4)      |
| Smoker                           | 50 (20.7)      |
| Opium use                        | 29 (12.0)      |
| Alcohol use                      | 0.0 (0.0)      |
| Amphetamine                      | 10 (4.1)       |
| Hypertension                     | 77 (32.0)      |
| Hyperlipidemia                   | 21 (8.7)       |
| Diabetes mellitus                | 47 (19.5)      |
| Renal insufficiency              | 32 (13.3)      |
| Chronic lung disease             | 4 (1.7)        |
| Cerebrovascular disease          | 20 (8.3)       |
| Peripheral vascular disease      | 2 (0.8)        |
| Prior CAD                        | 48 (19.9)      |
| Prior CHF                        | 24 (10.0)      |
| Prior CABG                       | 12 (5.0)       |
| Prior PCI                        | 3 (1.2)        |
| Economic status                  |                |
| Low                              | 94 (39.0)      |
| Moderate                         | 145 (60.2)     |
| High                             | 2 (0.8)        |
| Age, years (Mean ± SD)           | 66.00 ± 16.5   |

CAD: Coronary artery disease; SCA/SCD: Sudden cardiac arrest/sudden cardiac death; CHF: Congestive heart failure; CABG: Coronary artery bypass graft; PCI: Percutaneous coronary intervention

Table 2. Clinical characteristics of enrolled patients with sudden cardiac arrest/sudden cardiac death

| Characteristics                  | n (%)          |
|----------------------------------|----------------|
| NYHA functional class            |                |
| No symptoms                      | 31 (12.9)      |
| I                                | 42 (17.4)      |
| II                               | 99 (41.1)      |
| III                              | 56 (23.2)      |
| IV                               | 13 (5.4)       |
| Activity                         |                |
| Low                              | 110 (45.6)     |
| Moderate                         | 83 (34.4)      |
| High                             | 48 (19.9)      |
| Depression                       |                |
| Low                              | 135 (56)       |
| Moderate                         | 88 (36.5)      |
| Severe                           | 18 (7.5)       |
| Quality of life                  |                |
| Low                              | 114 (47.3)     |
| Moderate                         | 124 (51.5)     |
| High                             | 3 (1.2)        |

NYHA: New York Health Association

Cardiopulmonary resuscitation was unsuccessful in 195 (80.9%) patients. Among the groups with successful and unsuccessful CPR there were not statistically significant differences in age, sex, and presence of previous heart disease. The presenting arrhythmia in admission was significantly different between two groups and pulseless electrical...
activity/asystole was more common in the group with unsuccessful CPR (Table 5).

Considering study population, 75 (31.1%) patients were female. The mean age was not significantly different between men and women. Moreover, there were no significant sex differences in prevalence of hyperlipidemia, diabetes mellitus, family history of CAD, renal insufficiency, chronic lung disease, cerebrovascular disease, prior coronary artery disease, prior congestive heart failure, or severe left ventricular systolic dysfunction. Women were more likely to have hypertension and men more likely to be smoker. Men were more asymptomatic than women before SCD/SCA event; also they had more physical activity. ECG at admission (pulseless electrical activity/asystole vs. ventricular tachycardia/ventricular fibrillation) and successfulness of CPR was not significantly different between men and women (Table 6).

Table 5. Relationship between successfulness of cardiopulmonary resuscitation and patients’ characteristics

| Patients’ characteristics | Successful CPR | Unsuccessful CPR | P     |
|--------------------------|----------------|------------------|-------|
| Total number             | 46 (19.1)      | 195 (80.9)       | 1.000 |
| Males                    | 32 (69.6)      | 134 (68.7)       |       |
| Smoking                  | 9 (19.6)       | 41 (21.0)        |       |
| Hypertension             | 21 (45.7)      | 56 (28.7)        | 0.035 |
| Hyperlipidemia           | 3 (6.5)        | 18 (9.2)         | 0.773 |
| Diabetes mellitus        | 10 (21.7)      | 37 (19.0)        | 0.681 |
| Renal insufficiency      | 8 (17.4)       | 24 (12.3)        | 0.343 |
| Chronic lung disease     | 2 (4.3)        | 2 (1.0)          | 0.166 |
| Cerebrovascular disease  | 1 (2.2)        | 19 (9.7)         | 0.136 |
| Peripheral vascular disease | 0 (0.0)    | 2 (1.0)          | 1.000 |
| Prior coronary artery disease | 14 (30.4) | 34 (17.4)        | 0.063 |
| Prior congestive heart failure | 4 (8.7)    | 20 (10.3)        | 1.000 |
| Left ventricular EF ≤ 35% | 8 (17.4)  | 42 (21.5)        | 0.330 |
| Electrocardiogram in admission | 59.9 ±16.6 | 63.2 ± 16.9      | 0.228 |

CPR: Cardio pulmonary resuscitation; EF: Ejection fraction; BBB: Bundle branch block; AF: Atrial fibrillation, STEMI: ST-elevation myocardial infarction

Table 6. Baseline and cardiac arrest characteristics of men and women with sudden cardiac arrest/sudden cardiac death

| Characteristics | Men n (% in sex) | Women n (% in sex) | P     |
|-----------------|-----------------|-------------------|-------|
| Total number of sex | 166             | 75                | -     |
| Family history of CAD | 9 (5.4)       | 17 (22.7)         | 0.661 |
| Smoking         | 42 (25.3)       | 8 (10.7)          | 0.010 |
| Hypertension    | 41 (24.7)       | 36 (48.0)         | 0.001 |
| Hyperlipidemia  | 14 (8.4)        | 7 (9.3)           | 0.809 |
| Diabetes mellitus | 27 (16.3)  | 20 (26.7)         | 0.078 |
| Renal insufficiency | 23 (13.9)  | 9 (12.0)          | 0.838 |
| Chronic lung disease | 3 (1.8)      | 1 (1.3)           | 1.000 |
| Cerebrovascular disease | 10 (6.0)    | 10 (13.3)         | 0.057 |
| Prior coronary artery disease | 35 (21.1) | 13 (17.3)        | 0.602 |
| Prior congestive heart failure | 18 (10.8)  | 6 (8.0)           | 0.644 |
| No prior symptoms | 29 (17.5)      | 2 (2.7)           | 0.034 |
| High activity in life | 44 (26.5)  | 4 (5.3)           | 0.001 |
| Ejection fraction ≤ 35% | 33 (19.9)  | 17 (22.7)         | 0.570 |
| Electrocardiogram in admission | -             | -                 | 0.778 |
| Pulseless electrical activity/asystole | 91 (54.8) | 39 (52.0)        |       |
| Ventricular tachycardia/fibrillation | 38 (22.9) | 15 (20.0)        |       |
| Other (STEMI, BBB, AF rhythm) | 37 (22.3) | 21 (28.0)        |       |
| Unsuccessful CPR | 134 (80.7)     | 61 (81.3)         | 1.000 |
| Age, years (Mean ± SD) | 61.51 ±16.9 | 64.95 ± 16.7     | 0.144 |

CAD: Coronary artery disease; BBB: Bundle branch block; AF: Atrial fibrillation, STEMI: ST-elevation myocardial infarction; CPR: Cardio pulmonary resuscitation
In study population, 23 (9.5%) patients were under 40 years old (17 to 39 years). Among these group of patients, 19 (82.6%) were male, 5 (21.7%) were smoker, 5 (21.7%) were opium user, 6 (26.1%) were amphetamine user and, and no one was alcohol user. None had any positive history of SCA/SCD, hypertension, diabetes mellitus, peripheral vascular disease, cerebrovascular disease, and/or prior coronary artery disease. The congestive heart failure was detected in 3 (13.0%) patients before the SCD incidence, and one of them was amphetamine user. The NYHA class was two or more in 8 (34.8%) patients. The presenting arrhythmia was predominantly pulseless electrical activity or asystole which was seen in 14 (60.9%) of patients under 40 years old. Two patients had ST-elevated myocardial infarction (STEMI) in first ECG. Long QT syndrome or Brugada pattern was not seen in any patients. Among these 23 young patients with SCA/SCD, only two patients (8.7%) were resuscitated successfully, which one of them had STEMI and the other had asystole in the first ECG.

**Discussion**

The mean age of affected patients with SCA/SCD in this study was similar to previous reports; in the mid-60s. The prevalence of atherosclerotic risk factors was also similar. Depression has been shown to have a relationship with SCD in some studies. In our results, 44% of patients had moderate or severe depressive mode according to family members idea. Among the patients, only 19.9% and 10.0% had known coronary artery disease and prior congestive heart failure, respectively. These percentages were lower than similar studies. Severe LV systolic dysfunction was presented in 20.7% of patients. In the majority of cases, SCD was the first manifestation.

In out-of-hospital cardiac arrest, up to 40% of the initial arrhythmias were either VT or VF. In some of recent studies, pulseless electrical activity/asystole was found in 52% of patients versus 48% for VT/VF. Pulseless electrical activity cases have been compared with VT/VF cases; they were older, more likely to be female, and importantly less likely to have hospital discharge (6% versus 25%). In this study, presenting arrhythmia was pulseless electrical activity or asystole which was seen in 130 (53.9%) of patients and cardiopulmonary resuscitation was unsuccessful in 195 (80.9%) of patients.

In this study, women were more likely to have hypertension and men more likely to be smoker with no significant sex differences in prevalence of hyperlipidemia, diabetes mellitus, family history of CAD, renal insufficiency, chronic lung disease, cerebrovascular disease, prior coronary artery disease, prior congestive heart failure, or severe left ventricular systolic dysfunction. But in some published studies, women were less likely than men to have a previous diagnosis of coronary artery disease or left ventricular dysfunction. Therefore, they may be less eligible to receive an ICD. Forensic examination of SCD cases is not mandatory in Iran; hence, first relatives may refuse further post-mortem evaluation. But the cause of sudden unexplained death of the young persons before 40 is very important for those who left behind. Arrhythmic death in this age group is often caused by familial disease and every effort should be made to find the probable cause of SCD.

**Study limitations**

The main limitation was observational nature of this study and the results must be viewed as hypothesis-generating only. The second limitation was the low number of patients that can be recruited in another study.

**Conclusion**

Unexpected cardiac arrests and/or unexpected cardiac deaths are a major health concern, but the true magnitude of it still remains unknown to the public, and the rate of successful cardiopulmonary resuscitation is low. Reduced EF may be an independent predictor of sudden cardiac death in some patients but it is not enough. Concerning the fact that ICDs can save lives, we are still in need of more effective risk stratification and prevention methods for those vast groups of patients experiencing SCD. As a result, it is recommended that pooled data from large population-based studies of SCD might be useful to find more candidates for ICD implantation.

**Acknowledgements**

This study was approved and supported by Shahid Beheshti University of Medical Sciences.

**Conflict of Interests**

Authors have no conflict of interests.

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How to cite this article: Sadeghi R, Adnani N, Sohrabi MR, Alipour Parsa S. Risk of sudden cardiac death. ARYA Atheroscler 2013; 9(5): 274-9.