



## ARAŞTIRMA / RESEARCH

# Sudden death and coronary heart disease: a retrospective autopsy study

Ani ölüm ve koroner kalp hastalığı: geriye dönük bir otopsi çalışması

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### Abstract

**Purpose:** The aim of this study was to examine how often myocardial infarction in abruptly dying persons with or without known coronary heart disease could be found as well as to estimate the severity of atherosclerosis in correlation to gender and age.

**Materials and Methods:** A retrospective study was designed using data from clinical records of 184 cases of adults who submitted with sudden death and underwent autopsy during a period of one year. We studied the demographic characteristics, season and location of death. Symptoms, smoking, alcohol and drug use, circumstances of death were also record. Coronary arteries findings in autopsy, heart weight, localization of myocardial infarction and the presence of an old myocardial infarction were record from autopsy report.

**Results:** 92 patients (54 male, 38 female mean aged 64.8 years) met the inclusion criteria. In the majority of cases an acute myocardial infarction was certified during autopsy (92.4%). Grading severity of coronary arteries lesions in most of cases they characterized as severe (75%), and only in two cases they found to be normal. Males were more possible to have moderate or severe lesions in coronary arteries compared with females. Severe atherosclerosis was found in older victims more frequent compare to younger.

**Conclusions:** Acute myocardial infarction is a common autopsy finding among victims of sudden cardiac death. Old-aged myocardial infarction also can be identified in many cases and the severity of atheromatic lesions extends by age.

**Key words:** Sudden death, coronary heart disease, autopsy, myocardial infarction.

### Öz

**Amaç:** Bu çalışmada, bilinen koroner kalp hastalığı olan veya olmayan ve aniden ölen kişilerde miyokard enfarktüsünün ne sıklıkta bulunduğunu belirlenmesi ve aterosklerozun ciddiyetinin cinsiyet ve yaşla ilişkisinin saptanması amaçlanmıştır.

**Gereç ve Yöntem:** Bir yıl içinde ani ölüm sonrası otopsi yapılan 184 erişkin olgunun klinik kayıtlarından elde edilen veriler kullanılarak retrospektif bir çalışma tasarlanmıştır. Demografik özellikleri, mevsimi ve ölüm yerleri incelendi. Semptomlar, sigara, alkol ve uyuşturucu kullanımı ile ölüm koşulları da kaydedildi. Koroner arter bulguları, kalp ağırlığı, miyokard enfarktüsünün lokalizasyonu ve eski miyokard enfarktüsü varlığı otopsi raporlarından alınmıştır.

**Bulgular:** 92 hasta (54 erkek, 38 kadın, yaş ortalaması 64,8), çalışmaya dahil edilme kriterlerini karşıladı. Otopsi sırasında olguların çoğunda (%92,4) akut miyokard enfarktüsü onaylandı. Saptanan olgularda koroner arter lezyonlarının derecelendirme şiddetleri; çoğunda şiddetli (%75) ve sadece iki vakada normal olarak tespit edildi. Erkeklerin, koroner arterlerde kadınlara göre orta veya şiddetli lezyonlara sahip olma olasılığı daha yüksekti. Yaşlı kurbanlarda şiddetli ateroskleroz daha sık saptanmıştır.

**Sonuç:** Akut miyokard enfeksiyonu, ani kardiyak ölümü kurbanları arasında yaygın bir otopsi bulgusudur. Yaşlı miyokard enfeksiyonu da birçok vakada tanımlanabilir ve aterosklerotik lezyonların şiddeti yaşa göre artabilir.

**Anahtar kelimeler:** Ani ölüm, koroner kalp hastalığı, otopsi, miyokard enfarktüsü, ateroskleroz

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## INTRODUCTION

Cardiovascular disease is a major cause of death and the most common cause of death in developed countries<sup>1</sup>. Sudden cardiac death (SCD) accounts two-thirds of all cardiovascular deaths and several studies estimate an incidence of SCD of 36 –128 deaths per 100 000 person-years with the majority of cases due to coronary disease<sup>2,3</sup>. SCD accounts for 50% of all Coronary Heart Disease (CHD) deaths and 15% to 20% of all deaths, but the true incidence of SCD varies among countries, depends on study population and methods used among studies and greatly remains unclear<sup>4</sup>.

A large proportion of SCD cases are due to CHD<sup>5</sup>. Other causes of SCD include inherited structural heart diseases such as hypertrophic cardiomyopathy<sup>6</sup>, dilated cardiomyopathy<sup>7</sup> and structural disorders as arrhythmogenic right ventricular cardiomyopathy<sup>8</sup>, anomalous origin of a coronary artery, cardiac tumors, valvular heart disease and inflammatory processes such as sarcoid and myocarditis. In the absence of structural heart disease, SCD should occur due to primary electrical diseases- intriguing ion channel disorders, that include long QT syndrome (LQTS), Brugada syndrome and catecholaminergic polymorphic ventricular tachycardia (CPVT)<sup>9</sup>.

Autopsy in victims of sudden cardiac death plays a significant role to investigate whether death was due to cardiac causes or not (e.g drug abuse), to identify the nature of cardiac disease as the underline cause of SCD (arrhythmic or structural heart disease) and to establish if an inherited heart disease exists<sup>10</sup>. Finally it should be mentioned, that in some cases of sudden death the underline anatomic problem is never identified<sup>11</sup>.

The main interest in this study is to examine whether and how often myocardial infarction could be identified in abruptly dying persons with or without known coronary heart disease as well to estimate the severity of atheromatosis in correlation to gender and age.

## MATERIALS AND METHODS

A retrospective study was designed using data from clinical records of 184 cases of adults aged >20 years old who admitted with sudden death and underwent autopsy in laboratory of forensic

medicine and toxicology of Aristotle University of Thessaloniki during a period of one year (2013). Sudden death was defined as an unexpected, not injury death of a previous free of symptoms person with or without preexisting heart disease either within 1 hour of symptom onset (when event was witnessed) or within 24 hours of having been observed alive and symptom free (unwitnessed event)<sup>12,13</sup>.

Each potential source of medical information utilized, such as pre and post mortem medical report, toxicology report, referral specialist report, as with information given by victim relatives. Two independent researchers examined all information relevant to autopsy to determine whether cases fulfilled study inclusion criteria. Classification of unwitnessed deaths was a very difficult issue and cases with no access to their medical history and no other information were excluded from study. Black and Hispanic populations also excluded from study population because they have different risk for SCD compared to white populations. Where consensus could not be reached, third independent review was sought from a professor of Forensic medicine.

Finally 92 cases met the inclusion criteria and took part in study. Demographic characteristics (age and gender), season and location of death were collected and studied. Instead of body mass index, a semi quantitative method was used to estimate weight and victims characterized as severely underweight, underweight, normal (healthy weight), overweight, obese Class I (Moderately obese), obese Class II (Severely obese) and obese Class III (Very severely obese). International Classification of Primary Care (ICPC-2) was used for the classification of diseases of past medical history. Symptoms, smoking, alcohol and drug use, circumstances of death (during exercise or not) were recorded from the information collected as it was we described previously. Coronary arteries findings in autopsy, heart weight, localization of myocardial infarction and the presence of an old myocardial infarction were recorded from autopsy report. The presence of acute coronary thrombi and myocardial infarction was documented macroscopically. The age of the myocardial and coronary lesions was estimated by observing morphological characteristics changing with time. This study was approved by the local ethics committee and was carried out in accordance with the World Medical Association's Declaration of Helsinki.

### Statistical analysis

All analyses were performed with SPSS 21 software. Statistics are reported as mean and SD, median with interquartile range or counts (%). Normality test has been done and variables were compared with the parametric t-test or the nonparametric Mann-Whitney U test, as it was appropriate. Chi-square and the Fisher's exact test were used to account differences for categorical variables.

### RESULTS

During the year 2013 a total of 92 patients (54 male-58%, 38 female-41%, mean aged 64.8 years-SD:15.6

years) who met the inclusion criteria underwent an autopsy (Table 1). Males were younger (63.4 years-old SD:14.14) than female victims of sudden death (66.68 years-old SD:17.48-P=0.032). Most of deaths occurred in autumn (38 cases-41.3%). Investigating death's condition we found that most deaths occurred at rest (68 cases-73.9%), 17 cases (18.5%) during exercise and in 4 cases (4.3%) when victim slept. Regarding the place of death this was happened in most cases in victim's home (41 cases-44.6%) and the victim was characterized as normal weighted (33 cases-35.9%). In 41.3%(38 cases) victim was an active smoker, in 34.8%(32 cases) had alcohol consumption and in two cases was a toxin user (Table 1).

**Table 1. Baseline characteristics**

Variables	overall (n = 92)
Age in years, (mean $\pm$ SD )	64.8 $\pm$ 15.6
Gender n (%)	N (%)
Male,	54(57.8%)
Female	38(41.3%)
Weight n (%)	
severely underweight	1(1.1%)
underweight	2(2.2%)
normal (healthy weight)	33(35.9%)
overweight	32(34.8%)
obese Class I (Moderately obese)	19(20.7%)
obese Class II (Severely obese)	5(5.4%)
obese Class III (Very severely obese)	0(0%)
Season n (%)	
autumn,	38 (41.3%)
summer	31 (33.7%),
spring	14 (15.2%)
winter	9 (9.8%)
Symptoms n (%)	
fainting	32 (34.8%)
weakness	12 (13%)
dyspnea	12 (13%)
chest pain	9 (9.8%)
abdominal pain	3 (3.3%)
vomiting	7 (7.6%)
pallor	3 (3.3%)
febrile,	1 (1.1%)
hemoptysis	1 (1.1%)
indigestion	1 (1.1%)
No symptom or sign could be identified.	39 (42.4%)
Place of death n (%)	
Hospital	16(17.4%)
Home	41(44.6%)
Other	35(38%)
Conditions n (%)	
Rest	68(73.9%)
Exercise	17(18.5%)

Sleep	4(4.3%)
Smoking status n (%)	
No smoker	34(37%)
Previous smoker	8(8.7%)
Unknown	12(13.0%)
Current smoker	38(41.3%)
Alcohol n (%)	
Yes	32(34.8%)
No	49(53.3%)
Unknown	11(12.0%)
Toxins n (%)	
Yes	2(2.2%)
No	77(83.7%)
Unknown	11(12.0%)

The leading sign reported before death was an episode of fainting (32 cases-34.8%). Others symptoms or signs that were reported was weakness (12 cases-13%), dyspnea (12 cases-13%), chest pain (9 cases-9.8%), abdominal pain (3 cases-3.3%), vomiting (7 cases- 7.6%), pallor (3 cases-3.3%) and in one case febrile, hemoptysis and indigestion was reported. In 39 cases (42.4%) no symptom or sign

could be identified (Table 1). After classification victim' s of sudden death previous diseases with International Classification of Primary Care, ICPC-2-E, it was found that most cases had disorders of circulatory system-codes K 74-96(51 cases-55.4%), 15 cases(16.3%) had a positive for coronary artery disease family history and 20 cases (21.7%) had no past medical history (Table 2).

**Table 2. Classification of diagnosis from past medical history**

International Classification of Primary Care, ICPC-2-E	Cases-N%
circulatory system-codes K 74-96	51 (55.4%)
respiratory system codes R 95-96	6 (6.5%)
renal – urinary system codes U 02-77	4 (4.3%)
gastrointestinal system codes D 85-98	7 (7.6%)
bones codes L 3-91	3 (3.3%)
psychiatric disorders code P 70	2 (2.2%)
endocrinology and metabolism disorders codes T82-90	28(30.4%)
positive for coronary artery disease family history	15 (16.3%)
no past medical history	20 (21.7%)

In the majority of cases an acute myocardial infarction was certified during autopsy (85 cases-92.4%) and in one case myocardial ischemia without myocardial infarction was found. An infraction of anterior wall of Left Ventricle (LV) was identified in 56 cases (60.9%), an infraction of posterior wall of LV in 52 cases(56.5%) and an infraction of interventricular septum (ivs) in 34 cases (37%). Grading severity of coronary arteries lesions in most of cases they characterized as severe (69 cases-75%), as moderate in 18 cases (19.6%), as mild in 3 cases and only in two cases they found to be normal. A macroscopic examination of coronary vessels found a clot in 7 cases (7.6%). In 4 cases clot was found in right coronary artery and in one case was found in

left anterior descending artery and in left circumflex artery respectively. Finally in one case additionally to clot presence, a left main artery division was noticed (Table 3). Similarly in one case death occurred by a valve occlusion and in two cases (2.2%) a broken heart was found. Hearts mean weight was 478,23 gr (SD: 147,4 gr). No relation between gender and myocardial infarction location was detected, but males was more possible to have moderate or severe lesions in coronary arteries compared with females (P=0.01). In cases with atheromatic lesions, severe atheromatosis was found in older victims (67.68 years-old SD:13.64) more frequent compare to younger (56.13 years-old SD: 18.07-P= 0.009) and normal autopsy findings in coronary arteries was

commonly found in younger compared to older victims (37.00 years-old SD:5.65/ 65.41 years-old SD : 15.19 P=0.01). Additionally, there was no statistical significant difference in age among victims

with acute myocardial infraction (P=0.180). Moreover, myocardial infraction location had no relation to victim's age (anterior P=0.083, posterior P=0.622, ivs P=0.318) (Table 3).

**Table 3. Findings of coronary heart disease and a comparison by age and gender**

Variables	N (%)	Gender Differences Male/female P value	Differences by age Mean age (years-old) P value
Atheromatic lesions			
severe	69(75%)	44/25 P=NS	67,68 yo SD:13,64 P=0,009
moderate	18(19,6%)	P=NS	P=NS
mild	3(3,3%)	P=NS	P=NS
normal	2(2,2%)	0/2 P=NS	37,00 yo SD:5,65 P=0,01
moderate-severe	87(94,6%)	54/33 P=0,01	65,95 yo SD:14,63 P=0,002
Acute myocardial infraction	85(92,4%)	48/37 P=NS	65,15 yo SD:15,88 P=NS
Old-aged myocardial infraction	59(64,1%)	40/19 P=0,029	65,56 yo SD:14,62 P=NS
Location of myocardial infarction			
Anterior wall	56(60,9%)	38/18 P=0,059	63,69 yo SD:16,62 P=NS
Posterior wall	52(56,5%)	32/20 NS	65,19 yo SD:15,68 P=NS
Interventricular septum	34(37%)	17/17 P=NS	63,64 yo SD:16,53 P=NS
Presence of clot	7(7,6%)	P=NS	P=NS
RCA	4(4,3%)		
LAD	1(1,1%)		
LCx	1(1,1%)		
Co-existing LMA deviation	1(1,1%)		

NS=Not Significant (P>0.05), SD= Standard Deviation,

LAD: Left Anterior Descending, LCx: Left Circumflex, RCA: Right Coronary Artery LMA: Left Main coronary Artery

## DISCUSSION

In the present study the mean age of victims was 64.8 years (SD: 15.6 years) and the majority of cases with SCD were male. The incidence of SCD increases with age regardless of sex or race<sup>14</sup>. Women have lower incidence of SCD probably because of the protection they enjoy from coronary atherosclerosis before menopause<sup>15</sup>. Results from a study carried out in Greece also showed that men had a higher incidence of coronary atherosclerosis than women, but with advancing age (>60 years) this difference was reduced<sup>16</sup>. Former studies identified a diurnal and a seasonal pattern of SCD. Morning hours (with the exception of sleep apnea syndrome related SCD) and winter months have been described to have a high risk of SCD<sup>17</sup>. These patterns were not confirmed in the present study.

Symptoms related to SCD have been separated in four temporal perspectives: prodromes (chest pain, palpitations, dyspnea, lightheadedness, fatigability), symptoms and signs of onset of terminal event (arrhythmia, hypotension, chest pain, dyspnea, lightheadedness), symptoms and signs of cardiac

arrest (loss of effective circulation and loss of consciousness) and symptoms and signs of biologic death (failure of resuscitation or failure of electrical, mechanical or central nervous system function after initial resuscitation)<sup>18</sup>. Some victims experience no symptoms before cardiac arrest, which was the most common state in the current study.

Obesity accelerates the progression of coronary atherosclerosis, but in the present study population obesity trends were low<sup>19</sup>. In most cases there was a history of cigarette smoking and alcohol consumption. Smoking increases twofold to threefold the risk of sudden death<sup>20</sup>. On the other hand mild to moderate alcohol consumption was associated with a reduced risk of SCD among women<sup>21</sup>. Severe atheromatosis was found in older victims more frequent compare to younger and normal autopsy findings in coronary arteries was more common in younger compared to older victim. It is well established that CHD is a silent and progressive process, but lesions can be found even in young people<sup>22</sup>.

Almost in two-third of cases in the study, an old-aged myocardial infarction was identified. Old myocardial infarction is one of the most important pathological manifestations in sudden cardiac death. Fatal arrhythmia arising from a fibrotic scar has been implicated as the cause of SCD in cases with old myocardial infarction, but Takada et al. showed that a new coronary plaque rupture independent of the old infarct was a major cause of sudden cardiac death with old myocardial infarction<sup>23</sup>. Michalodimitrakis et al. investigating 445 cases of SCD in adults who underwent autopsy found at least one coronary artery had evidence of moderate to advanced atherosclerosis. Fifty-eight cases (13.0%) had coronary thrombi, mostly involving the left anterior descending and the right coronary arteries (81%), but only six of these were associated with acute myocardial infarction<sup>16</sup>, suggesting that fatal arrhythmias was the most common cause of SCD in this study. More close to findings of Farb et al. it was found in 57% of cases of sudden coronary death acute changes in coronary plaque morphology (thrombus, plaque disruption, or both). In hearts with myocardial scars and no acute infarction, active coronary lesions were identified in 46% of cases. Neither myocardial infarction nor an active coronary lesion was present in 19% of cases<sup>24</sup>.

Di Maio et al. in an autopsy study found macroscopically thrombus in 13.4% of the cases of SCD<sup>25</sup>, but Davies and Thomas identified coronary thrombi in 74% of cases using post-mortem angiography and histological examinations in cases of SCD<sup>26</sup>. On the other hand it has to be stressed that myocardial necrosis may not be apparent by light microscopy for several hours after the critical ischemic event. So we have to accept that differences in incidence of myocardial infarction, in thrombus presence and in prevalence of myocardial necrosis, depend on methods used in each study, on different ways they assess the coronary circulation and on different inclusion criteria that were used. Finally in one case in our study spontaneous coronary artery dissection occurred in RCA with clot presence. Spontaneous coronary artery dissection is a rare cause of acute myocardial infarction is more common in younger patients and in women and can lead to SCD<sup>27</sup>.

In the present retrospective study there were difficulties with missing data from patients' medical records. An effort made by the researchers to overcome bias related to autopsy examiner by using

guidelines for autopsy investigation of SCD<sup>10</sup>. A major limitation of the study is the absence of histologic examination, which unfortunately was not available. The relatively small sample size produces limitations in external and internal validity of the study. In addition, the presence of confounding variables, such as pulmonary embolism and acute aortic dissection may affect study's results.

Acute myocardial infarction is a common autopsy finding among victims of SCD. Old-aged myocardial infarction also can be identified in many cases and the severity of atheromatic lesions extends by age. Primary and secondary prevention of SCD include strategies to correct and prevent modified risk factors for CHD and SCD.

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