

An Overview of the Relationship between Early-Onset Myocardial Infarction and Family History

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Abstract

Background: Sudden Cardiac Death (SCD) and Acute Coronary Syndrome (ACS) are major public health concerns, particularly in individuals with a family history of early-onset Coronary Artery Disease (CAD).

Objectives: The impact of family history on ACS and SCD risk remains underexplored.

Methods: This retrospective study included 689 patients diagnosed with ST-Elevation Myocardial Infarction (STEMI) who underwent Primary Percutaneous Coronary Intervention (PPCI) between January 2011 and June 2015. Patients with a parental history of SCD due to Myocardial Infarction (MI) were identified (n = 29, 4.2%). Demographic data, cardiovascular risk factors, and angiographic findings were evaluated.

Results: The median age at STEMI onset in patients with a parental history of SCD was 49 (41.5-52) years, 8.9 years younger than their parents' age at SCD. Most patients were male (96%) and smokers (83%). Hyperlipidemia was present in 80%, although only 7% had been previously diagnosed. Multi-vessel disease was observed in 80%, and 28% required Coronary Artery Bypass Grafting (CABG). Two patients (7%) died due to cardiogenic shock.

Conclusion: Patients with a parental history of SCD develop STEMI at younger ages. Smoking and low HDL levels were key risk factors. Early screening and preventive measures, including smoking cessation and lipid control, were essential for high-risk individuals. Further studies are needed to explore genetic predisposition and targeted prevention strategies.

Keywords: Sudden Cardiac Death, Acute Coronary Syndrome, Family History, ST-Elevation Myocardial Infarction, Cardiovascular Risk Factors

1. Background

Coronary Artery Disease (CAD) is the leading cause of morbidity and mortality worldwide despite advances in diagnosis and treatment.¹⁻³ Acute Coronary Syndrome (ACS), often caused by atherosclerotic plaque rupture and thrombus formation, can lead to Myocardial Infarction (MI) or Sudden Cardiac Death (SCD).¹

Sudden cardiac death is defined as an unexpected death occurring within one hour of symptom onset, or within 24 hours if unwitnessed, without a non-cardiac cause.^{2,3} Although SCD incidence is relatively low in young individuals, it rises sharply with age, especially after 80 years.^{4,5} Globally, millions die annually due to ACS and SCD, predominantly in people older than 35 years.⁶

Family history is a recognized non-modifiable risk factor for CAD and SCD, particularly when onset occurs at a young age.^{7,8} Genetic predisposition, including inherited

lipid disorders and arrhythmia syndromes, plays an important role in early disease manifestation.⁹⁻¹² Studies show that offspring of individuals who suffered SCD have increased risk for cardiovascular events.¹³

2. Objectives

Despite existing research, the combined effect of family history and traditional risk factors on young-onset myocardial infarction and SCD remains insufficiently explored. Understanding these relationships is critical for identifying high-risk individuals who may benefit from early screening and preventive measures. SCD not only typically occurs during individuals' most productive years, but it is also notably increasing among younger age groups.^{14,15} This increase is believed to be related to the transmission of CAD across generations, leading to earlier manifestations of the disease in each successive generation, especially when combined with other risk factors.

This study aims to evaluate clinical and laboratory characteristics of patients with CAD according to the presence or absence of a parental history of SCD, and to identify potential risk factors that may help refine early diagnosis and prevention strategies.

3. Methods

This retrospective study was approved by the Institutional Review Board (IRB) of Mudanya University (Date: 01.10.2024, Decision no: 2024-05). Due to the retrospective nature of the study, the requirement for informed consent was waived. All patient data were anonymized and handled confidentially in accordance with the Declaration of Helsinki. In this study, 689 patients diagnosed with STEMI and treated with Primary Percutaneous Coronary Intervention (PPCI) between January 2011 and June 2015 were evaluated.

Patients with a history of SCD in one of their parents, who developed STEMI and underwent PPCI, were included in the study. Information on parental SCD was primarily obtained from patient interviews at admission. Patients with missing medical records or those whose parents' sudden death was due to causes other than MI were excluded.

STEMI diagnosis was based on the presence of ≥ 1 mm ST-segment elevation in the Electrocardiogram (ECG) and significant elevation in cardiac troponin levels. Coronary angiography findings were also used to confirm STEMI.

The history of SCD in the parents was verified through patient records and information obtained from family members. However, detailed data regarding parental smoking history, lipid profiles, and other cardiovascular risk factors were not available.

Demographic data (age, gender), clinical characteristics (smoking, lipid profile, hypertension, diabetes), and angiographic findings (presence of multi-vessel disease)

were recorded for all patients. Multivessel disease was defined as the presence of $\geq 70\%$ stenosis in two or more major epicardial coronary arteries or their major branches on coronary angiography.

3.1. Statistical Analysis

Statistical analyses were limited to descriptive statistics. Continuous variables are presented as mean \pm Standard Deviation (SD) or range, and categorical variables are expressed as counts and percentages.

Continuous variables were tested for normality using the Shapiro–Wilk test. As the data were not normally distributed, they were expressed as median with Interquartile Range (IQR) and compared between groups using the Mann–Whitney U test. Categorical variables were expressed as counts and percentages, and differences between groups were evaluated using the Chi-square test or Fisher's exact test, as appropriate. For subgroup analysis, the study population was divided into two age groups: Group 1 (≤ 45 years) and Group 2 (>45 years). A P -value <0.05 was considered statistically significant.

4. Results

In our study, 4% ($n = 29$) of STEMI patients had a history of SCD in one or both parents. The median age of these patients at STEMI was 49 years (IQR: 41.5–52), while the median age of their parents at SCD was 57.9 years (IQR: 51–64) (Table 1). Most patients (90%, $n = 26$) experienced STEMI earlier than their parents' age at SCD, with a median difference of 8.9 years. Only 10% ($n = 3$) had STEMI at an older age than their fathers' SCD.

Among the patients, 83% ($n = 24$) had paternal SCD history, and 17% ($n = 5$) had maternal SCD history. Forty-one percent ($n = 12$) had STEMI before 45 years of age, whereas only 10% ($n = 3$) of their parents experienced SCD before 45.

Table 1. Baseline Characteristics of the Study Population

Variable	Value
Age, years (median, IQR)	49 (41.5-52)
Male, n (%)	28 (96%)
Hypertension, n (%)	6 (22%)
Diabetes mellitus, n (%)	3 (11%)
Hyperlipidemia, n (%)	2 (7%)
Cigarette smoking, n (%)	24 (83%)
Father sudden death by history of CAD, n (%)	24 (83%)
Mother sudden death by history of CAD, n (%)	5 (17%)
Sudden death of parents age, years (median, IQR)	57.9 (51-64)
LDL cholesterol, mg/dl (median, IQR)	143.8 (81-217)
HDL cholesterol, mg/dl (median, IQR)	33.8 (23-53)
Total cholesterol, mg/dl (median, IQR)	205.7 (132-298)
Triglycerides, mg/dl (median, IQR)	175.3 (67-403)
Fasting glucose, mg/dl (median, IQR)	138.3 (89-381)
Creatinine, mg/dl (median, IQR)	0.96 (0.7-1.4)
Ejection fraction (EF), % (median, IQR)	49.8 (25-65)

CAD: Coronary artery disease; LDL: Low-density lipoprotein; HDL: High-density lipoprotein.

Table 2. Cardiovascular Events

Variable	n (%)
Anterior MI	16 (55)
Inferior MI	13 (45)
PCI in non-infarct-related arteries	5 (18)
Heart failure	6 (20)
Arrhythmia (VT, VF)	5 (18)
Multivessel disease	23 (80)
CABG	8 (28)
Mitral valve repair	1 (3)
Mortality	2 (7)
ICD implantation	1 (3)

MI: Myocardial infarction; PCI: Percutaneous coronary intervention; VT: Ventricular tachycardia; VF: Ventricular fibrillation; CABG: Coronary artery bypass grafting; ICD: Implantable cardioverter-defibrillator.

Of those undergoing primary PCI, 96% (n = 28) were male, and 4% (n = 1) female. The female patient was 41 years old, had anterior MI, smoked, and had family history of MI-related SCD in her father (54 years) and brother (43 years).

Anterior MI was present in 16 patients, and inferior MI in 13. Multi-vessel disease was detected in 23 patients (Table 2). Five patients underwent elective PCI for non-infarct-related arteries, and eight were referred for coronary artery bypass surgery. Ventricular fibrillation occurred in five patients before PCI. One patient required intubation after sudden cardiac arrest two months post-PCI, with an open stent and inducible ventricular tachycardia; an implantable cardioverter-defibrillator was recommended. Another patient was advised mitral valve repair due to ischemic cardiomyopathy-related severe mitral regurgitation.

Two patients died from cardiogenic shock: a 68-year-old whose father also died from MI at the same age, and a 49-year-old whose father had SCD at 60. Smoking was the most common cardiovascular risk factor, present in 83% (n = 24). The mean LDL and HDL cholesterol levels were 143.8 mg/dl and 33.8 mg/dl, respectively (Table 1). Although 80% had hyperlipidemia, only 7% were diagnosed before STEMI. Two male patients had no cardiovascular risk factors other than family history; both had maternal SCD history with HDL levels of 38 mg/dl and 27 mg/dl.

Statistical comparisons were performed between the defined age groups (Group 1: ≤ 45 years; Group 2: > 45 years) for all evaluated parameters, including baseline demographic and clinical characteristics (age, sex, hypertension, diabetes mellitus, hyperlipidemia, cigarette smoking, family history of sudden cardiac death, lipid profile, fasting glucose, creatinine, and ejection fraction). Continuous variables were analyzed using the Mann-Whitney U test and categorical variables using the Chi-square or Fisher's exact test, as appropriate. No statistically significant differences were observed between age groups for any of the evaluated parameters (all *P*-values > 0.05).

5. Discussion

Cardiovascular Diseases (CVD) have long been recognized as the leading cause of mortality and morbidity world wide, with Coronary Artery Disease (CAD) accounting for 42% of all CVD-related deaths.⁵ In the United States, the average age for first MI presentation is 65 years in men and 70 years in women, with 83% of CAD-related deaths occurring in individuals aged 65 or older.⁶ According to the Euroaspire III study, Turkey has the highest incidence of MI under age 50 in Europe, with average MI ages of 50 for men and 60 for women. The study also noted that urban residents experience MI approximately eight years earlier than rural residents.⁷

In our cohort, the median age of patients with ST-Elevation Myocardial Infarction (STEMI) was 49 (41.5-52), years, significantly younger than the average age of SCD in their parents, which was 57.9 (51-64) years. Most patients (96%) were male. While the reasons for earlier STEMI onset compared to parental SCD remain unclear, incomplete data on parental risk factors limit firm conclusions. It is plausible that patients have accumulated more substantial risk factors, with smoking and low High-Density Lipoprotein (HDL) levels emerging as prominent contributors, especially among males.

Although Acute Myocardial Infarction (AMI) is relatively uncommon under age 45 (2-6% of cases), its rising prevalence in younger adults is concerning due to premature mortality and long-term morbidity.^{8,9} Younger patients typically present with single-vessel atherosclerosis and STEMI. Despite generally favorable short-term prognosis, these patients face worse long-term outcomes.¹⁰ In this study, 41% of patients experienced STEMI before 45, while only 10% of their parents had SCD before 45.

Smoking was identified as the leading risk factor for early MI both in the Euroaspire III study and our cohort, where 83% of STEMI patients were smokers.⁷ According to the Turkish Adult Risk Factor Study (TEKHARF), 59.4% of Turkish men and 18.9% of women smoke.^{11,12} The Eastern European region, including Turkey, contributes to 25% of global tobacco-related deaths.¹³

Family history remains a critical non-modifiable risk

factor for CAD, as highlighted by the National Cholesterol Education Program Adult Treatment Panel (NCEP-ATP) III guidelines.^{14,15} The INTERHEART study further identified abnormal lipid profiles, smoking, hypertension, diabetes, obesity, psychosocial factors, poor diet, alcohol consumption, and physical inactivity as major MI contributors globally.¹⁶ Among STEMI patients, smoking was most common (68%), followed by hypertension (57.8%), dyslipidemia (47.5%), and diabetes (37.7%).¹⁶ Gender differences exist, with hypertension, diabetes, and dyslipidemia predominating in women, and smoking in men.¹⁷ Dyslipidemia, especially low HDL levels, was highly prevalent (68.6%).¹⁷ MI risk advances by 8.3, 12.4, and 11.5 years earlier in presence of hypertension, total cholesterol/HDL ratio ≥ 5.5 , or heavy smoking, respectively.¹⁸ A Turkish study confirmed the critical roles of family history, smoking, and low HDL in young adults.¹⁹

In our study, smoking (83%), hyperlipidemia (80%), hypertension (22%), and diabetes mellitus (11%) were the most frequent cardiovascular risk factors. Notably, only 7% of patients were aware of their hyperlipidemia diagnosis before STEMI, and 91% of those diagnosed were unaware of their lipid parameters. The average LDL cholesterol was 143.8 mg/dl, and average HDL was 33.8 mg/dl, with 75% of patients exhibiting HDL levels below 40 mg/dl. Although parental lipid profiles were largely unknown, the high prevalence of low HDL in offspring may reflect both genetic predisposition and environmental influences such as smoking, diet, and physical inactivity. Low HDL may be partly inherited through genes regulating lipid metabolism, but lifestyle factors significantly modulate HDL levels and cardiovascular risk.

Patients with a family history of CAD often exhibit more severe disease,²⁰ as seen in our cohort where 80% had multi-vessel disease, 27% underwent elective percutaneous coronary intervention (PCI) in non-infarct-related arteries, and 28% received Coronary Artery Bypass Grafting (CABG). Two patients died due to cardiogenic shock, one required Implantable Cardioverter-Defibrillator (ICD) implantation, and another underwent mitral valve repair.

Our findings underscore the necessity of early diagnosis and follow-up programs targeting individuals with parental history of sudden cardiac death. Preventive strategies focusing on smoking cessation, improving HDL levels, and lipid monitoring could be effective in reducing cardiovascular risk. Furthermore, earlier screening and incorporation of genetic testing for familial risk factors may enable targeted interventions to reduce morbidity and mortality in this high-risk population.

5.1. Limitations

The small sample size was a limiting factor in this study. In addition, the characterization of cardiovascular risk

factors in parents who experienced sudden cardiac death was incomplete due to lack of detailed data. The verification of parental SCD was mainly based on patient or family reports, without access to official death certificates or autopsy results, which may affect accuracy. Furthermore, the absence of a control group limits the ability to specifically attribute the findings to a familial history of SCD. The study population was predominantly male (96%), limiting the ability to perform meaningful gender-based analyses. Future studies with larger cohorts and control groups are needed to strengthen the evidence.

6. Conclusion

This study identified that male offspring with a history of parental SCD experienced STEMI at younger ages than their parents. Smoking and low HDL cholesterol levels were the most prominent modifiable risk factors in this group, with many patients unaware of their lipid status prior to STEMI. These findings underscore the need for proactive cardiovascular risk screening—especially lipid profiling and smoking status assessment—in individuals with a family history of SCD, beginning earlier than current guidelines suggest. Healthcare providers should implement targeted smoking cessation programs and initiate early lipid-lowering interventions when indicated. Moreover, integrating genetic counseling and testing into routine care for these high-risk individuals may facilitate personalized preventive strategies. Such measures could effectively reduce premature STEMI incidence and improve long-term cardiovascular outcomes.

Research Highlights

What Is Already Known?

- Early onset of STEMI is observed in patients with a family history of SCD.
- Paternal SCD history is more commonly reported than maternal history.
- Traditional cardiovascular risk factors, such as smoking and hyperlipidemia, are important contributors to early STEMI but often remain undiagnosed.

What Does This Study Add?

- STEMI before age 45 occurred in 41% of patients, significantly higher than the 10% of parents with SCD before this age.
- Multi-vessel disease and serious complications were prevalent in this patient group.
- Despite high rates of smoking and hyperlipidemia, awareness and prior diagnosis of lipid abnormalities were low.

Author Contributions

AD, NA, and MCB participated in designing the study and provided the data. AD, NA, HG, and MCB performed statistical modeling and tabulated the results, and wrote the first draft of the paper. AD, NA, MCB, and MB helped in writing the final manuscript and discussing the results. All

authors read and approved the final manuscript.

Conflict of Interest Disclosures

All authors declared that they have no conflict of interest.

Ethical Approval

Ethics committee approval was obtained from the local ethics committee (Date: 01.10.2024, Decision no: 2024-05).

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