

# Younger age of patients with myocardial infarction correlates with higher number of relatives with history of premature atherosclerosis

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## Research article

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# Abstract

**Background.** Premature coronary artery disease belongs to the most pressing global issues in a modern cardiology. Family history appears to be one of the most important and significant risk factors in young patients with myocardial infarction (MI). The aim of the study was to investigate the role of family history of premature cardiovascular disease (CVD) in patients <50 years with myocardial infarction (MI) compared to patients  $\geq 50$  years with MI and to young healthy people.

**Methods.** The studied group (MI<50) consisted of 240 patients aged 26-49 years with MI. The control groups consisted of 240 patients (MI $\geq$ 50) with MI aged 50-92 years and 240 healthy people aged 30-49 years.

**Results.** There were statistically significant differences between the MI<50 and MI $\geq$ 50 and young healthy groups regarding family history of premature MI/ischaemic stroke and percent of patients with of  $\geq 2$  relatives affected including parents, children, siblings, siblings of parents and grandparents (10.8%, 2.9%, 3.7%, respectively;  $p < 0.0001$ ). There was a statistically significant negative correlation between the age of the first episode of MI and the number of relatives with a history of premature MI/stroke ( $r = 0.249$ ,  $p < 0.05$ ) within all MI patients. Statistically significant differences between MI<50 and MI $\geq$ 50 groups as well as young healthy control group were revealed regarding prevalence of smoking, body mass index (BMI), LDL, HDL, triglycerides (TG) and glucose levels.

**Conclusions.** Younger age of patients with myocardial infarction correlates with a higher number of relatives with a history of premature MI/ischemic stroke. Thus, the family history of premature atherosclerosis involving not only the first-, but also the second-degree relatives, seems to be valuable and could be considered in an individual CVD risk evaluation in young people.

## Background

Coronary artery disease (CAD), according to the report of the American Heart Association, remains the leading cause of cardiovascular diseases (CVD) deaths [1]. Regarding this, premature CAD seems to be one of the most pressing global issues in this area.

Data regarding the prevalence of myocardial infarction (MI) in young people differ according to assumptive cut-off age and study population. The percent of patients aged < 35 years who underwent cardiac catheterization due to MI was determined to be 2% [2]. Recently published data reported 10% of patients with MI, ST-elevation MI (STEMI), non-ST elevation MI (NSTEMI), and unstable angina (UA) were  $\leq 40$  years of age [3]. Patients aged < 40 years represented 1.2% of all patients with MI in a Polish study [4]. When a cut-off age of 45 was established, the percent of patients increased to 3.2% [5]. The percent of adults aged < 55 years with MI within participants of the Global Registry of Acute Coronary Events (GRACE) was 23 [6]. In one of the recently published meta-analysis the cut-off age for young age of acute coronary syndrome (ACS) has been set down on the level of 50 [7].

Family history appears to be one of the most important and significant risk factors in young patients with MI. It covers inherited genetic as well as environmental risk factors (diet, lifestyle, smoking). A recently published Polish study (the MAGNETIC Project) revealed that young adults with a family history of premature CAD presented unfavourable dietary patterns, which suggested the possible continuity of familial lifestyle across generations [8].

A family history of premature CV events is defined as MI or ischaemic stroke in the first degree relatives at age < 55 years in men and < 65 years in women [9, 10]. The INTERHEART study indicated that parental history of CAD was a risk factor independent of environmental, cultural, behavioural, classical, and genetic conditions [11]. Furthermore, the age of onset of disease in parents and whether one or both parents are affected is valuable information providing an assessment of individual risk of MI. Nevertheless, the data regarding the role of a history of premature CV events in family members other than parents are scarce.

The aim of the study was to analyse risk factors for MI at young age, particularly the role of a family history of CVD. Regarding the plenty of cut-off ages for young MI among the literature, we assumed this limit on the level of 50 years. We investigated the family history of premature MI/ischaemic stroke in patients with MI at age < 50 compared to patients with MI at age  $\geq$  50 and to healthy young people. We assessed correlations between the number of relatives affected and the age of MI patients, including not only parents but also other family members such as siblings, grandmothers, grandfathers, children and siblings of parents.

## Methods

### Patients

The investigated population included 720 people, partly participants of the previously published study [12].

The studied group consisted of 240 young patients aged < 50 years (mean age 43.5, SD  $\pm$  5.0; range 26–49) admitted to the Department of Cardiology, Centre of Postgraduate Medical Education, Grochowski Hospital (Warsaw) with the first episode of MI diagnosed based on ST changes in ECG including STEMI (ST elevation MI) as well as NSTEMI (non-ST elevation MI), serum troponin levels and clinical manifestation. The group (MI < 50 group) consisted of 188 men and 52 women (78.3% and 21.7%, respectively).

The data from studied group have been compared to the control group (MI  $\geq$  50 group) including also 240 patients admitted to our department due to the first episode of MI, aged  $\geq$  50 years, range 50–92 (mean 65.9 years, SD  $\pm$  12.6), including 152 men and 88 women (63.3% and 36.7%, respectively).

The another control group consisted of healthy young people, aged, similarly to the studied group < 50 years (mean 43.2 years, SD  $\pm$  5.0, range from 30 to 49 years), without history of CAD. This group

(young healthy controls) included 137 men and 103 women (57.1% and 42.9%, respectively). These participants were recruited in the Regional Blood Centre and a general practitioner outpatient clinic.

We collected from all participants of the study (together 720 people) detailed information regarding family history of premature CVD (MI/ischaemic stroke in men aged < 55 and in women aged < 65), body mass index (BMI), smoking, hypertension, diabetes mellitus (DM) and depression. Hypertension was defined, according to ESH/ESC (European Society of Hypertension, European Society of Cardiology) guidelines as values  $\geq 140$  mmHg of systolic blood pressure (SBP) and/or  $\geq 90$  mmHg of diastolic blood pressure (DBP), based on blood pressure measurement, medical history and ongoing blood pressure-lowering treatment [13]. DM was assessed accordingly to WHO and ADA (American Diabetes Association) guidelines based on a fasting plasma glucose  $\geq 126$  mg/dl or  $\geq 200$  mg/dl in an oral glucose tolerance test measurements, based on medical history and hypoglycaemic ongoing treatment [14].

The investigation conforms to the principles outlined in the Declaration of Helsinki. The study protocol was approved by the Ethical Committee of the Centre of Postgraduate Medical Education. The participants gave written informed consent for participation in the study.

## **Biochemical analyses**

The blood for all biochemical analyses, including glucose, total cholesterol, HDL and LDL cholesterol and triglyceride (TG) plasma concentrations was taken in the first morning after admission to the hospital. Analyses were determined from fasting blood samples by standard enzymatic methods using COBAS INTEGRA 800 reagents and equipment (Roche Diagnostics GmbH, Mannheim, GE).

## **Statistical analysis**

The comparison of the studied groups was performed using the U Mann-Whitney test, p values were corrected for multiple comparisons, and the level of significance was established at 0.05. Correlations were assessed using Spearman's test for abnormal data distribution. Statistical analyses were performed using the Statistica software package (StatSoft Inc., Tulsa, USA).

## **Results**

### **Clinical and metabolic characteristics of the studied groups**

There were statistically significant higher prevalence of smoking (86.4% vs 64.2%,  $p < 0.0001$ ), BMI ( $28.6 \text{ kg/m}^2$  vs  $27.6 \text{ kg/m}^2$ ,  $p = 0.0114$ ), total cholesterol (210.0 mg% vs 197.7 mg%,  $p = 0.0065$ ), LDL cholesterol (133.6 mg% vs 124.5 mg%,  $p = 0.0394$ ) and triglyceride levels (180.4 mg% vs 127.7 mg%,  $p < 0.0001$ ) in the MI < 50 group compared to the MI  $\geq 50$  group (Table 1). HDL cholesterol (41.5 mg% vs 47.6 mg%,  $p < 0.0001$ ), glucose at admission (134.4 vs 159.6 mg%,  $p = 0.0004$ ) and fasting glucose (106.0 mg% vs 116.4 mg%,  $p = 0.0056$ ) levels were significantly lower in the MI < 50 group compared to the MI  $\geq 50$  group.

There were no statistically significant differences between these groups in previous diagnoses of hypertension (55.9% in MI < 50 group and 69.6% in MI ≥ 50 group), DM (19.8% vs. 35.7%) or depression (8.5% vs. 7.9%, respectively).

Statistically significant differences between the MI < 50 group and the young healthy group included smoking (86.4% vs 43.1%, respectively,  $p < 0.0001$ ), BMI (28.6 kg/m<sup>2</sup> vs 27.0 kg/m<sup>2</sup>,  $p = 0.0001$ ), hypertension (55.9% vs 29.6%,  $p < 0.0001$ ), DM (19.8% vs 1.6%,  $p < 0.0001$ ) and depression (8.5% vs 3.7%,  $p = 0.017$ ) as well as LDL cholesterol (133.6 mg% vs 122.6 mg%,  $p = 0.0259$ ), HDL cholesterol (41.5 mg% vs 54.8 mg%,  $p < 0.0001$ ), TG (180.4 mg% vs 134.1 mg%,  $p = 0.0007$ ) and fasting glucose (106.0 mg% vs 95.6 mg%,  $p = 0.0093$ ) levels. There were no differences between these groups in total cholesterol level (210.0 mg% vs 203.5 mg%, respectively). There were no individuals using or addicted to cocaine, HIV infected or affected by other severe conditions nor within studied group of MI < 50 or both control groups of MI ≥ 50 and young healthy people.

## **Socio-economic characteristics of the studied groups**

There were no significant differences between MI < 50 and MI ≥ 50 in the level of education (primary, vocation, secondary or university) or the type of job (unemployed, blue collar, white collar or pensioners). There was a statistically significant difference in a marital status (percent of married people: 74.9% in MI < 50 vs 64.1% in MI ≥ 50 group,  $p = 0.04$ ) between these groups (Table 2).

Comparing the MI < 50 group and the young healthy control group, there was a statistically significant difference in the level of education (percent of people with university degree: 22.1% vs 41.4%, respectively,  $p < 0.0001$ ). Although, patients with premature MI were less commonly employed as white collars compared with young healthy people, there were no differences between these groups in the type of job as well as in a marital status.

## **Family history**

There were statistically significant differences between MI < 50, MI ≥ 50, and the young healthy group in the presence of a family history of premature CVD in the first-degree relatives: 32.9% vs 9.6% ( $p < 0.0001$ ) and 32.9% vs 11.7% ( $p < 0.0001$ ), respectively (Table 3). There were also statistically significant differences between MI < 50, MI ≥ 50 and the young healthy group in the presence of a family history of premature CVD age involving the first- and the second-degree relatives: 35.9% in MI < 50 group vs 15.6% in MI ≥ 50 ( $p < 0.0001$ ) and 14.2% in young healthy controls ( $p < 0.0001$ ). Moreover, there were statistically significant differences between studied groups in the family history of CVD events within family members (the first- and the second-degree relatives) for each age category – 65.4% in MI < 50 group vs 47.6% in MI ≥ 50 ( $p < 0.0001$ ) and 41.7% in young healthy controls ( $p < 0.0001$ ).

The statistically significant differences between MI < 50, MI ≥ 50 and young healthy groups also included percent of patients with ≥ 2 affected relatives – parents, children, siblings, siblings of parents, grandparents – with a history of premature CVD events: 10.8% vs 2.9% ( $p < 0.0001$ ) and 10.8% vs 3.7% ( $p < 0.0001$ ), respectively; Fig. 1.

There was a statistically significant negative correlation between the age of the first episode of MI and the number of the first-degree relatives with a history of premature MI/stroke ( $r = 0.249$ ,  $p < 0.05$ ) within all MI patients (Fig. 2). There was also a clear correlation between the age of MI and the number of affected the first- and the second-degree relatives with premature CVD events ( $r = 0.208$ ,  $p < 0.05$ ), the number of the first- degree relatives with CVD event in each age category ( $r = 0.235$ ,  $p < 0.05$ ) and the number of the first- and the- second degree relatives with CVD events at every age ( $r = 0.193$ ,  $p < 0.05$ ).

## Discussion

In our study there was a significantly higher incidence of a family history of premature CVD events in patients with MI age  $< 50$  in comparison to patients with MI at age  $\geq 50$  and to healthy young people. Family history is a CAD risk factor independent from other risk factors. In the Malmo Diet and Cancer Study, family history of coronary heart disease (CHD) was associated with an incidence of CHD with a hazard ratio of 1.52 (95%CI: 1.39–1.65), and only a small proportion of the family history effect was mediated by hypertension, hyperlipidaemia and diabetes [15].

Although the highest cardiovascular risk was associated with a maternal history at age  $< 50$  years and a paternal history at age  $< 55$  years, no substantial differences were seen between maternal and paternal positive CVD history [16]. In a Dutch Cohort study a particularly high incidence of CVD has been revealed in people with parental onset of MI before age 70, with maternal history of MI before age 60 being the strongest predictor of CVD incidence [17].

Offspring age of onset of CVD is significantly associated with both maternal and paternal age of CVD onset [18]. Nevertheless, data regarding the role of a family history of CVD that includes relatives other than parents or the number of affected family members are scarce.

In our study, there were significant differences between MI  $< 50$ , MI  $\geq 50$  group and young healthy controls in positive family history of CVD involving not only the prevalence of premature CVD events restricted to parents but also such events in other the first- and the second-degree relatives. Moreover, there were statistically significant differences between the studied groups in the prevalence of CVD events at every age in family members (the first- and the second-degree relatives). A higher number of relatives with a positive history of CAD, including parents, children, siblings, siblings of parents and grandparents, was associated with a younger age of MI.

Interestingly, there was a clear negative correlation between the age of the first MI and the number of relatives with premature CVD events, and this relationship was particularly evident in the analysis involving the first-degree relatives, but not exclusively. An Italian study revealed that being a relative (including parents, siblings and siblings of parents) of an early-onset MI case confers an adjusted hazard ratio of 2.7 for such events [19]. There are also data indicating that early-onset hypertension in grandparents raises the risk for hypertension in grandchildren, even after adjusting for early-onset hypertension in parents and for lifestyle factors [20].

Among other risk factors, the prevalence of smoking, BMI, HDL, LDL, TG and glucose levels differs significantly between the MI < 50 group and both control groups (MI ≥ 50 and healthy controls aged < 50) in our study. Such findings are independent of region and patient ethnicity across the literature [21, 22]. For instance, our data are in concordance with recently published data from New Zealand, conducted in a more complex population, including Caucasians, Maori and Pacific islanders [23]. Although, among the risk factors for MI at a young age, smoking, hyperlipidaemia and obesity are crucial, there are some differences in their distribution between particular groups of patients [24, 25]. For example, the strongest predictor of ACS in women ≤ 45 years of age was diabetes, with a 6-fold increase in risk [26]. Our study confirmed the significance of smoking, dyslipidaemia, obesity and carbohydrates metabolism disturbances as CAD risk factors.

The major limitation of our study is a relatively small number of patients, thus the findings are difficult to apply to a larger, more diverse population. On the other hand, the high homogeneity of the groups, limited to Polish population of a Caucasian race, could be of value regarding the potential population and racial differences in the pathogenesis of CAD, particularly taking into account heritable risk factors. The control group of young healthy blood donors, usually more educated and more conscious of lifestyle than general population, may not represent the community at large. On the other hand, the fact that donors stay free from CAD until the age of 50, whereas our young patients suffer from MI before this age, enhances the role of lifestyle in CAD prevention.

## Conclusions

This study revealed that the number of family members with premature CAD correlated with the age of the first episode of ACS. The utility of this findings seems to be important for an individual life-style changes interventions as a rational CVD prevention. Once a positive family history, particularly strengthened by such data, has been established, the health care provider can emphasise the increased likelihood of MI at a young age as a strong incentive for patient-dedicated improvement in adherence to healthy life style and medical regimen.

In conclusion, family history of an early MI or stroke is one of the most evident risk factors for MI at a young age apart from smoking, BMI, lipid and glucose levels. Younger age of MI is associated with a higher number of relatives with a history of premature atherosclerosis. Thus, the family history of premature atherosclerosis involving not only the first-, but also the second-degree relatives, seems to be valuable and could be considered in an individual CAD risk evaluation in young people.

## Abbreviations

ACS

acute coronary syndrome

ADA

American Diabetes Association

AHA  
American Heart Association  
BMI  
body mass index  
CAC  
coronary artery calcification  
CAD  
coronary artery disease  
CHD  
coronary heart disease  
CVD  
cardiovascular disease  
DBP  
diastolic blood pressure  
HDL  
high-density lipoprotein  
LDL  
low-density lipoprotein  
MI  
myocardial infarction  
NSTEMI  
non-ST elevation MI  
SBP  
systolic blood pressure  
STEMI  
ST elevation MI  
TG  
triglycerides  
UA  
unstable angina  
WHO  
World Health Organization

## **Declarations**

- Ethics approval and consent to participate

The participants gave written informed consent for participation in the study. The investigation conforms to the principles outlined in the Declaration of Helsinki and the study protocol was approved by the Ethical Committee of the Centre of Postgraduate Medical Education.

- Consent for publication

Not applicable

- Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

- Competing interests

The authors declare that they have no competing interests

- Funding

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- Authors' contributions

MA – conception and design of the study, data collection and analysis, interpretation of data, writing and revision of the manuscript

KNW – data collection and analysis

AM – data collection and analysis

AB – conception of the study, interpretation of data, revision of the manuscript

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Not applicable

## References

1. Virani SS, Alonso A, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, et al. Heart Disease and Stroke Statistics-2020 Update: A Report From the American Heart Association. *Circulation*. 2020;141:9 doi: 10.1161/CIR.0000000000000757.
2. Wolfe MW, Vacek JL. Myocardial infarction in the young. Angiographic features and risk factor analysis of patients with myocardial infarction at or before the age of 35 years. *Chest*. 1988;94:5.
3. Deora S, Kumar T, Ramalingam R, Nanjappa Manjunath C. Demographic and angiographic profile in premature cases of acute coronary syndrome: analysis of 820 young patients from South India. *Cardiovasc Diagn Ther*. 2016;6:3 doi: 10.21037/cdt.2016.03.05..

4. Trzeciak P, Wożakowska-Kapłon B, Niedziela J, Gierlotka M, Hawranek M, Lekston A et al. Comparison of Inhospital and 12- and 36-Month Outcomes After Acute Coronary Syndrome in Men Versus Women <40 Years (from the PL-ACS Registry). *Am J Cardiol.* 2016;118:9 doi: 10.1016/j.amjcard.2016.07.067.
5. Gierlotka M, Zdrojewski T, Wojtyniak B, Poloński L, Stokwiszewski J, Gąsior M et al. Incidence, treatment, in-hospital mortality and one-year outcomes of acute myocardial infarction in Poland in 2009-2012–nationwide AMI-PL database. *Kardiol Pol.* 2015;73:3 doi: 10.5603/KP.a2014.0213.
6. Awad HH, McManus DD, Anderson FA Jr, Gore JM, Goldberg RJ. Young patients hospitalized with an acute coronary syndrome. *Coron Artery Dis* 2013;24:1 doi: 10.1097/MCA.0b013e32835b0bf7.
7. Ma Q, Wang J, Jin J, Gao M, Liu F, Zhou S et al. Clinical characteristics and prognosis of acute coronary syndrome in young women and men: A systematic review and meta-analysis of prospective studies. *Int J Cardiol* 2017;228 doi: 10.1016/j.ijcard.2016.11.148.
8. Osadnik T, Pawlas N, Lonnie M, Osadnik K, Lejawa M, Wądołowska L et al. Family History of Premature Coronary Artery Disease (P-CAD)-A Non-Modifiable Risk Factor? Dietary Patterns of Young Healthy Offspring of P-CAD Patients: A Case-Control Study (MAGNETIC Project). *Nutrients* 2018;10 doi: 10.3390/nu10101488.
9. Williams RR, Hunt SC, Heiss G, Province MA, Bensen JT, Higgins M et al. Usefulness of Cardiovascular Family History Data for Population-Based Preventive Medicine and Medical Research (The Health Family Tree Study and The NHLBI Family Heart Study). *The American Journal of Cardiology* 2001;87:2.
10. Lloyd-Jones DM, Nam BH, D'Agostino RB, Sr, Levy D, Murabito JM, Wang TJ et al. Parental cardiovascular disease as a risk factor for cardiovascular disease in middle-aged adults: a prospective study of parents and offspring. *JAMA* 2004;291:18.
11. Chow CK, Islam S, Bautista L, Rumboldt Z, Yusufali A, Xie C et al. Parental history and myocardial infarction risk across the world: the INTERHEART Study. *J Am Coll Cardiol* 2011;57:5 doi: 10.1016/j.jacc.2010.07.054.
12. Ambroziak M, Kolanowska M, Bartoszewicz Z, Budaj A. Adiponectin gene variants and decreased adiponectin plasma levels are associated with the risk of myocardial infarction in young age. *Gene.* 2018;642 doi: 10.1016/j.gene.2017.11.064.
13. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *European Heart Journal* 2013;34:7 doi: 10.1097/01.hjh.0000431740.32696.cc.
14. American Diabetes Association. Standards of medical care in diabetes-2015 abridged for primary care providers. *Clin Diabetes.* 2015;33:2 doi: 10.2337/diaclin.33.2.97.
15. Fritz J, Shiffman D, Melander O, Tada H, Ulmer H. Metabolic Mediators of the Effects of Family History and Genetic Risk Score on Coronary Heart Disease-Findings From the Malmö Diet and Cancer Study. *J Am Heart Assoc* 2017;6:3 doi: 10.1161/JAHA.116.005254.

16. Weijmans M, van der Graaf Y, Reitsma JB, Visseren FL. Paternal or maternal history of cardiovascular disease and the risk of cardiovascular disease in offspring. A systematic review and meta-analysis. *Int J Cardiol* 2015;179: doi: 10.1016/j.ijcard.2014.11.017.
17. van Dis I, Kromhout D, Boer JM, Geleijnse JM, Verschuren WM. Paternal and maternal history of myocardial infarction and cardiovascular diseases incidence in a Dutch cohort of middle-aged persons. *PLoS One*. 2011;6:12 doi: 10.1371/journal.pone.0028697.
18. Allport SA, Kikah N, Abu Saif N, Ekokobe F, Atem FD. Parental Age of Onset of Cardiovascular Disease as a Predictor for Offspring Age of Onset of Cardiovascular Disease. *PLoS One* 2016;11:12 doi: 10.1371/journal.pone.0163334.
19. Cipriani V, Mannucci PM, Ardissino D, Ferrario M, Corsini G, Merlini PA. Familial Aggregation of Early-Onset Myocardial Infarction. *European Journal of Internal Medicine* 2010;21:6 doi: 10.1016/j.ejim.2010.07.017.
20. Niiranen TJ, McCabe EL, Larson MG, Henglin M, Lakdawala NK, Vasani RS et al. Risk for hypertension crosses generations in the community: a multi-generational cohort study. *Eur Heart J* 2017;38:29 doi: 10.1093/eurheartj/ehx134.
21. Sinha SK, Krishna V, Thakur R, Kumar A, Mishra V, Jha MJ et al. Acute myocardial infarction in very young adults: A clinical presentation, risk factors, hospital outcome index, and their angiographic characteristics in North India-AMIYA Study. *ARYA Atheroscler* 2017;13:2.
22. Lubiszewska B, Skóra E, Kruk M, Broda G, Ksiezzycka E, Kurjata P et al. Prevalence of classical risk factors in Polish women with premature coronary artery disease. *Kardiologia Polska* 2010;68:9.
23. Matsis K, Holley A, Al-Sinan A, Matsis P, Larsen PD, Harding SA. Differing Clinical Characteristics Between Young and Older Patients Presenting with Myocardial Infarction. *Heart Lung Circ* 2017;26:6 doi: 10.1016/j.hlc.2016.09.007.
24. Maroszyńska-Dmoch EM, Woźakowska-Kapłon B. Clinical and angiographic characteristics of coronary artery disease in young adults: a single centre study. *Kardiologia Polska* 2016;74:4 doi: 10.5603/KPa.2015.0178.
25. Soeiro Ade M, Fernandes FL, Soeiro MC, Serrano CV Jr, Oliveira MT Jr. Clinical characteristics and long-term progression of young patients with acute coronary syndrome in Brazil. *Einstein (Sao Paulo)* 2015;13:3 doi: 10.1590/S1679-45082015AO3381.
26. Bęćkowski M, Gierlotka M, Gąsior M, Poloński L, Zdrojewski T, Dąbrowski R et al. Risk factors predisposing to acute coronary syndromes in young women  $\leq 45$  years of age. *Int J Cardiol* 2018;264 doi: 10.1016/j.ijcard.2018.03.135.

## Tables

Table 1 Clinical characteristics of the studied groups: patients with MI aged <50 years (MI<50), patients with MI aged MI  $\geq 50$  years (MI  $\geq 50$ ) and healthy controls aged <50 years group (ns - not significant).

	MI<50	MI ≥50	Young healthy controls	p value	p value
	n=240	n=240	n=240		
	a	b	c	a vs b	a vs c
BMI (mean ±SD) kg/m <sup>2</sup>	28.6 ±4.4	27.6 ±4.0	27.0 ±4.3	0.0114	0.0001
Smoking n (%)	202 (86.4)	151 (64.2)	103 (43.1)	<0.0001	<0.0001
Hypertension n (%)	133 (55.9)	166 (69.7)	71 (29.6)	ns	<0.0001
Diabetes mellitus n (%)	47 (19.8)	86 (35.7)	4 (1.6)	ns	<0.0001
Depression n (%)	20 (8.5)	19 (7.9)	9 (3.7)	ns	0.017
Total cholesterol (mean ±SD) mg/dL	210.0 ±41.5	197.7 ±50.4	203.5 ±45.4	0.0065	ns
LDL (mean ±SD) m/dL	133.6 ±43.8	124.5 ±44.6	122.6 ±36.9	0.0394	0.0259
HDL (mean ±SD) mg/dL	41.5 ±12.8	47.6 ±18.0	54.8 ±22.0	<0.0001	<0.0001
TG (mean ±SD) mg/dL	180.4 ±128.9	127.7 ±71.2	134.1 ±82.4	<0.0001	0.0007
Glucose (mean ±SD) mg/dl	106.0 ±31.0	116.4 ±41.6	95.6 ±24.7	0.0056	0.0093

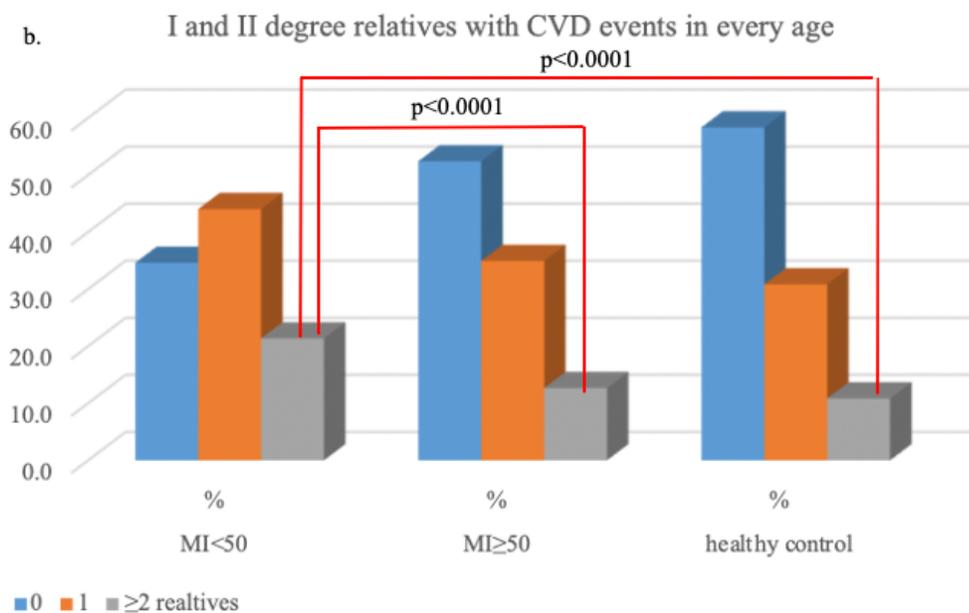
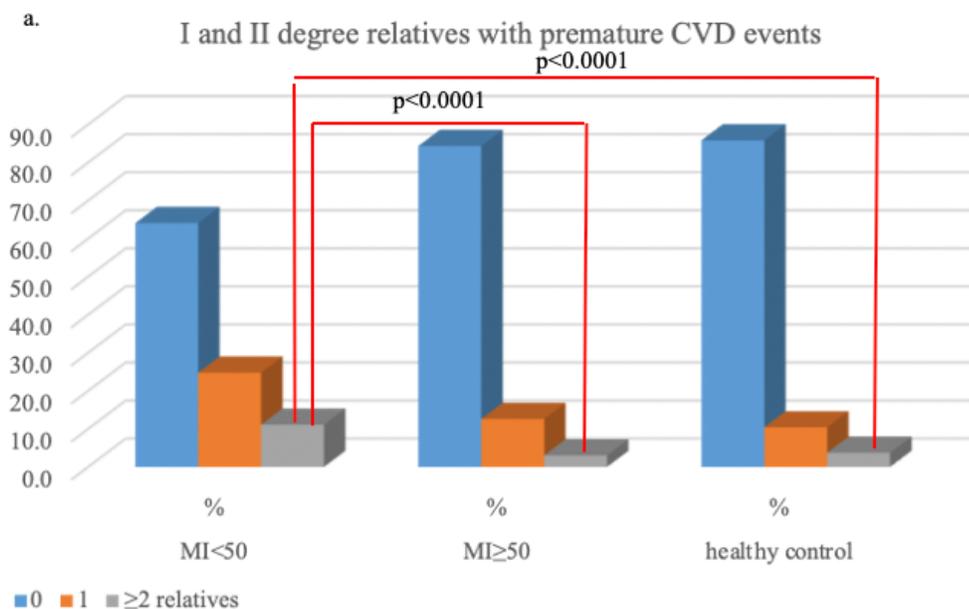
Table 2 Socio-economic status of the studied groups: patients with MI aged <50 years (MI<50), patients with MI aged MI ≥50 years (MI ≥50) and healthy controls aged <50 years group (ns - not significant).

	MI<50	MI ≥50	Young healthy controls	p value	p value
	n=240	n=240	n=240		
	a	b	c	a vs b	a vs c
Education level					
primary	14 (6.1)	37 (15.9)	6 (2.5)	ns	<0.0001
vocation	76 (32.9)	52 (22.3)	29 (12.2)		
secondary	90 (39.0)	102 (43.8)	104 (43.9)		
high	51 (22.1)	42 (18.0)	98 (41.4)		
Type of job					
unemployed	7 (3.2)	4 (1.8)	1 (0.5)	ns	ns
blue collar	108 (48.6)	94 (41.4)	84 (38.4)		
white collar	85 (38.3)	70 (30.8)	131 (59.8)		
pensioner	22 (9.9)	59 (26.0)	3 (1.4)		
Marriage status					
single	43 (19.3)	21 (8.9)	41 (17.1)	0.04	ns
married	167 (74.9)	152 (64.1)	181 (75.4)		
divorced	10 (4.5)	10 (4.2)	14 (5.8)		
widowed	3 (1.3)	54 (22.8)	4 (1.7)		

Table 3 Family history of premature CVD events (MI/ischaemic stroke in men aged <55 years and in women aged <65 years) in studied groups: patients with MI aged <50 years (MI<50), patients with MI aged MI ≥50 years (MI ≥50) and young healthy controls aged <50 years group.

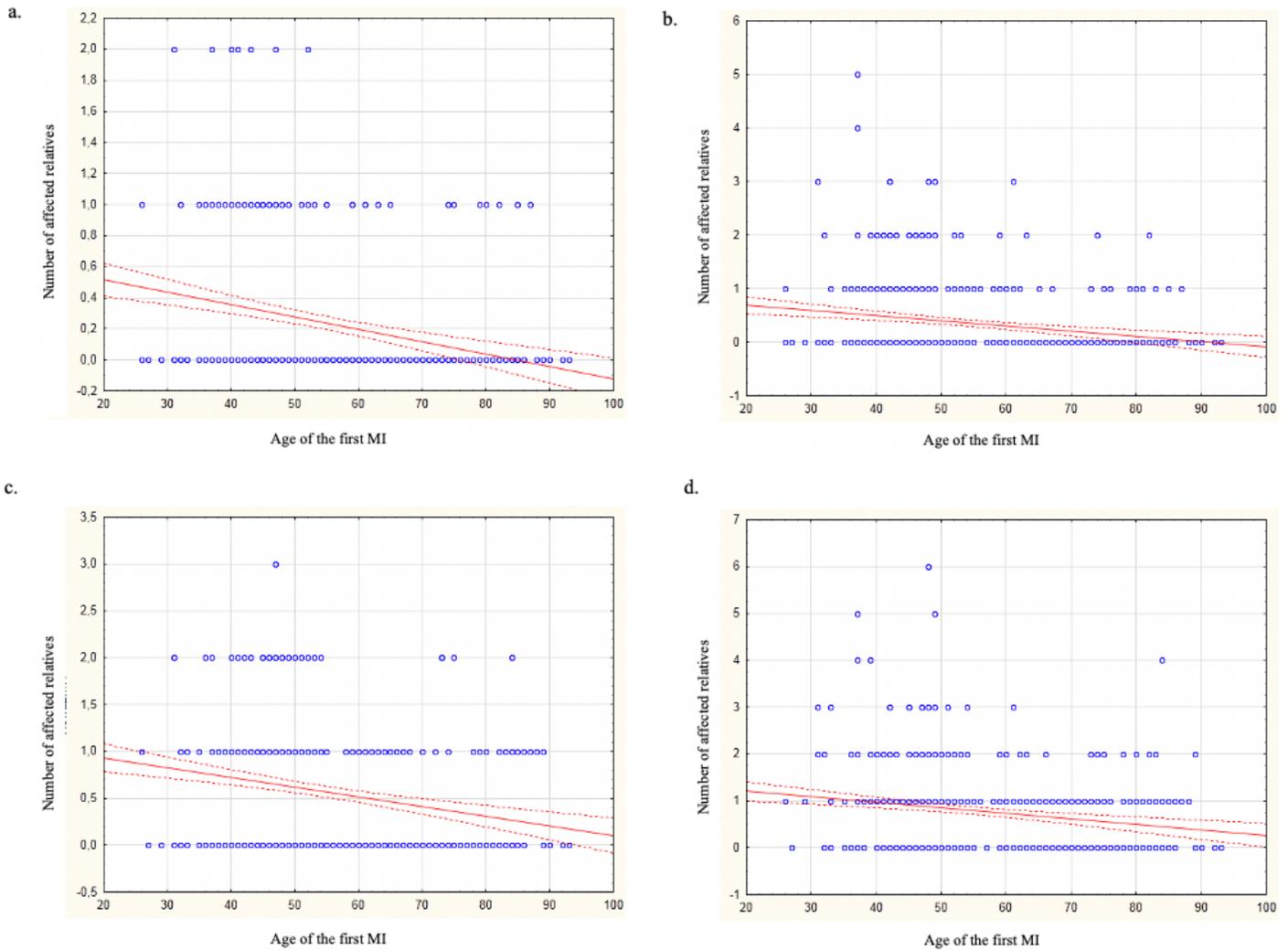
	MI<50 n=240	MI ≥50 n=240	Young healthy controls n=240	p value	p value
	a	b	c	a vs b	a vs c
Family history of MI/stroke in the first-degree relatives - all; n (%)	79 (32.9)	23 (9.6)	28 (11.7)	<0.0001	<0.0001
Family history of MI/stroke in the first-degree relatives - with ≥2 affected; n (%)	9 (3.7)	1 (0.4)	3 (1.2)	<0.0001	<0.0001
Family history of MI/stroke in the first- and the second- degree relatives - all; n (%)	84 (35.9)	36 (15.6)	34 (14.2)	<0.0001	<0.0001
Family history of MI/stroke in the first- and the second-degree relatives - with ≥2 affected; n (%)	26 (10.8)	7 (2.9)	9 (3.7)	<0.0001	<0.0001

## Figures



**Figure 1**

Differences between the MI<50, MI≥50 and young healthy control groups in the percent of cases with 0, 1 or ≥2 the first- and the second-degree relatives with the history of CVD events including: a. family history of premature CVD events: 11.1% MI<50 group vs 3% in MI ≥50 (p<0.0001) and 11.1% vs 3.7% in healthy young controls (p<0.0001); b. family history of CVD events at every age: 21.4% in MI<50 group vs 12.7% in MI ≥50 (p<0.0001) and 10.8% in healthy young controls (p<0.0001).



**Figure 2**

Correlations between the age of the patient first MI and the number of relatives with a history of CVD events: a. correlation between the age at the first MI and the number of the first-degree relatives with premature CVD events ( $r=0.249$ ,  $p<0.05$ ); b. correlation between the age at the first MI and the number of the first- and the second-degree relatives with premature CVD events ( $r=0.208$ ,  $p<0.05$ ); c. correlation between the number of the first-degree relatives and the number of relatives with CVD events at every age ( $r=0.235$ ,  $p<0.05$ ); d. correlation between the number of the first- and the second-degree relatives and the number of relatives with CVD events at every age ( $r=0.193$ ,  $p<0.05$ ).