

Association of traditional cardiovascular risk factors in adults younger than 55 years with coronary heart disease. Case-control study

SAGE Open Medicine

Volume 8: 1–6


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DOI: 10.1177/2050312120932703

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Abstract

Objectives: The traditional cardiovascular risk factors associated with coronary artery disease in individuals younger than 55 years old was determined in this study.

Methods: A retrospective, paired case–control study comprised of patients younger than 55 years old who were admitted to the hospital due to acute coronary syndrome with coronary artery disease from 2011 to 2016. There were two controls per case, paired by age, gender, admission date, and health insurance. Data from patients were collected, such as sociodemographic information, cardiovascular risk factors, and drug therapy information. A conditional logistic regression model was created to evaluate the association between traditional cardiovascular risk factors and coronary artery disease.

Results: There were 171 cases and 342 controls included in the study. The median age was 49 years, with a predominance of male gender (80.12%). Nearly 66% of cases had at least one traditional cardiovascular risk factor. The most common risk factors were obesity (57.31%), arterial hypertension (45.62%), and smoking (28.97%). Independent risk factors of coronary artery disease in patients younger than 55 years were arterial hypertension (odds ratio, 2.52; 95% confidence interval, 1.48–4.20; $p=0.001$) and smoking (odds ratio, 7.15; 95% confidence interval, 3.19–15.99; $p=0.00$). No significant association between diabetes mellitus and coronary heart disease in the global group (odds ratio, 2.04; 95% confidence interval, 0.91–4.58; $p=0.083$) was found.

Conclusion: For patients younger than 55 years, with a theoretically lower risk of coronary artery disease due to their age, having one or several traditional risk factors (smoking, arterial hypertension, dyslipidemia, or diabetes mellitus) confers an increased risk of coronary artery disease regardless of age.

Keywords

Risk factors, cardiovascular diseases, myocardial infarction, acute coronary syndrome, adult

Date received: 1 December 2019; accepted: 13 May 2020

Introduction

Acute myocardial infarction (AMI) is the leading cause of death worldwide.^{1,2} The vital statistics of the National Administrative Department of Statistics (DANE) of Colombia shows that coronary heart disease (CHD) is the leading cause of death which significantly affects the morbidity and mortality in different age groups.³

In young adults, the prevalence of CHD worldwide is 2%–3%.^{1,4} The risk of a recurrent AMI or fatal cardiovascular event is higher (17% of men and 21% of women) in the following 5 years after the first cardiovascular event in this

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*These authors takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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age group, with a similar risk of heart failure. This translates to a cost of 30 billion dollars per year and 6.8 million years of life lost in Latin America.⁵ The prevalence of CHD equates to a high economic cost with regard to health and impact on population productivity.

The traditional risk factors for AMI in the young population are smoking, dyslipidemia, diabetes mellitus, hypertension, and obesity.⁶ Recent studies have identified at least one traditional cardiovascular risk factor in this population.^{7–11} However, others have linked AMI in young adults with psychoactive substance abuse, hypercoagulable states, antiphospholipid syndrome, and family history of premature CHD. Since then, the importance of traditional risk factors in young patients became controversial.^{4,8,12}

Despite being a high-impact disease worldwide, only a few studies have evaluated the traditional risk factors of AMI in the young population in Colombia. Therefore, given the existing information gap, and the importance of epidemiology to implement primary and secondary prevention strategies, this study intends to evaluate the association of traditional cardiovascular factors in young adults with CHD.

Methods

A retrospective, paired case–control study of patients presenting with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI) with stenting implantation was carried out. This study gathered patients from Fundación Valle del Lili in Cali, Colombia, during the period between 1 January 2011 and 31 December 2016. From an ethical point of view, the study protocol was in accordance with the ethics guidelines of the Declaration of Helsinki and was approved by the ethics committee in institutional biomedical research of the hospital. This study was sponsored by the Fundación Valle del Lili. The ethics committee in biomedical research restricts the data related to this article used to support the findings. Data are available for researches fulfilling the criteria at <http://valledellili.org/tramites-ante-el-comite/>.

For this study, the cut-off age for the young male adult population was under 55 years.

This age cut-point was drawn from the recommendations of the National Cholesterol Education Program Third Adult Treatment Panel (ATP-III) and Seventh Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7).^{13,14} We also consider this value taking into account the age limit in the cardiovascular risk scales considered as premature CHD in men is less than 55 years old.^{15,16} Because almost 80% of the sample were men the same cutoff was applied for women. Cases were selected from the institutional register of interventional cardiology service. Only patients who were able to meet the following criteria were eligible: (1) age between 18 and 55 years; (2) diagnosis of ACS (unstable angina and AMI with or without ST-segment elevation); and (3) atherosclerotic CHD documented by angiography undergoing stenting (Supplemental Appendix 1).

Two controls were selected for each case. Patients from the institutional emergency register who presented a diagnosis of discharge unrelated to cardiovascular disease were included as controls. The cases were matched with controls by age, sex, admission date ± 5 days, and the same health insurance. The control that met all four characteristics was selected as the first possibility. Meanwhile, in cases where patients did not fit in all the variables, they were matched first by age and sex, then health insurance and finally the admission date.

We excluded all possible controls with a diagnosis of trauma, acute organ injury, and hemorrhagic shock that required surgical intervention. Sociodemographic data and traditional cardiovascular risk factors, such as diabetes mellitus, hypertension, dyslipidemia, smoking, familial history of CHD, alcoholism, previous cerebrovascular event, obesity (body mass index body mass index (BMI) $> 30 \text{ kg/m}^2$), use of cardiovascular drug therapy (angiotensin-converting enzyme inhibitors (ACEI), beta blockers, acetylsalicylic acid, and angiotensin receptor II blocker (ARB) were obtained from patients' clinical records. The indication of coronary heart angiography procedure and number of diseased vessels data were also considered.

There was a selection bias considering that control allocation and their access to health insurance are directly related to the socioeconomic status. Therefore, we matched the control that had the same health insurance accessibility (contributory, subsidized, and complementary medicine) as the case. On the contrary, we did not perform a sample size calculation because of the low number of cases, we collected all cases in the established period. A statistical power was calculated using the prevalence of dyslipidemia and arterial hypertension of 62.74% and 52.46%, respectively.

Statistical analysis

A univariate analysis of cardiovascular risk factors was performed. To evaluate the normality of the distribution of quantitative variables, we used the Shapiro–Wilk test. Variables that fulfilled normal distribution were presented as mean and standard deviation, otherwise, as median and interquartile range (IQR). Categorical variables were described as absolute values and percentages. Comparison tests were conducted through the use of Fisher's exact test for categorical variables and with t-test or Wilcoxon–Mann–Whitney test for quantitative variables. A univariate logistic regression analysis was used to determine the association of each traditional risk factor to CHD. Thereafter, the construction of multivariate conditional logistic regression model using the significant variables in the univariate analysis was made. In addition, the effect of age on the relationship of traditional cardiovascular risk factors and CHD was evaluated.

Results

There were 3788 patients with ACS with PCI from 1 January 2011 to 31 December 2016. Among these patients, 171 were

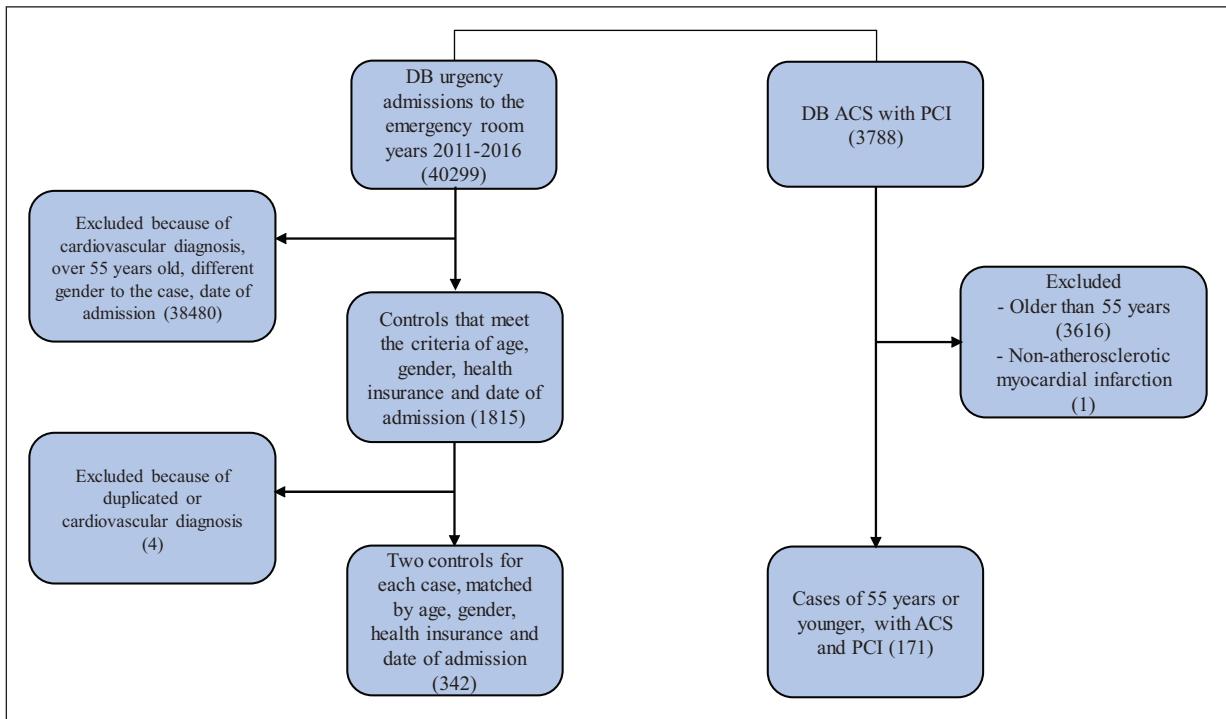


Figure 1. Flowchart of cases and controls included in the study. ACS: acute coronary syndrome; DB: database; PCI: percutaneous coronary intervention.

under 55 years old (4.51%) as shown in Figure 1. The median age was 49 years (IQR, 46–52 years); 76.61% were between 45 and 54 years, and 19.30% of the cases were women. There were 40,299 emergency admissions in the same age group, of which 1,819 controls met the inclusion criteria. Three-hundred forty-two matched controls were selected by age, sex, admission date, and health insurance to the case. There was no age difference between cases and controls. The difference in days of control admission to the case was 0 days (IQR, –4 to 4 days). The health insurance regime was contributory in 70% and subsidized in 24.62%, and the rest had an affiliation to complementary plans. The admission diagnoses of the controls are listed in Supplemental Appendix 2. Four controls were excluded and replaced because they matched the name and identification of the case, or by a cardiovascular diagnosis admission not detected in the initial evaluation, although different from ACS (Figure 1).

The prevalence of traditional cardiovascular risk factors (hypertension, diabetes mellitus, smoking, and obesity) was higher in cases than in controls as shown in Table 1. Also, 66% of cases had at least one traditional cardiovascular factor. On the contrary, more than 50% of the patients diagnosed with ACS already received pharmacological treatment. Of these patients, 38% were taking acetylsalicylic acid, 22.35% were taking beta blockers, 21.18% were taking ARB, and 14.79% were taking ACEI. Fifty-seven percent of cases had a single-vessel disease, 22.49% had two-vessel, and 20.12% had three-vessel disease during diagnostic angiography. We

identified only 9 of 171 (5.26%) cases with non-traditional cardiovascular risk factors (one with rheumatoid arthritis, one with chondrocalcinosis, one with chronic kidney disease, one with hyperhomocysteinemia, two patients with psychoactive substance abuse, one Takayasu disease, and two patients with human immunodeficiency virus infection (HIV).

Table 2 presents the univariate analysis of the association between CHD and traditional cardiovascular risk factors. Table 3 illustrates the multivariate conditional logistic regression model of CHD and conventional cardiovascular risk factors. Individuals under 55 years of age who had arterial hypertension, dyslipidemia, and diabetes mellitus and were into smoking and alcoholism were significantly associated with a higher probability of CHD in the univariate analysis, and hypertension and smoking were factors significantly associated with CHD in the multivariate analysis.

For patients aged 40–45 years (cases $n=31$), the main risk factor related to CHD was smoking (odds ratio [OR], 9.030, 95% confidence interval [CI], 1.68–48.51, $p=0.010$), and diabetes mellitus had a tendency to increase the probability of CHD but without statistical significance (OR, 10.011, 95% CI, 0.84–118.03, $p=0.067$). Individuals between 46 and 50 years whose risk factors were high blood pressure, diabetes mellitus, and smoking showed a significant association with CHD (OR, 5.798, 95% CI, 1.107–30.36, $p=0.037$ for diabetes mellitus; OR, 4.43, 95% CI, 1.61–12.17, $p=0.004$ for arterial hypertension; and OR, 5.166, 95% CI, 1.008–26.45, $p=0.049$ for smoking). For people older than

Table 1. Sociodemographic characteristics and previous medical history.

Variable	Cases (n = 171)	Controls (n = 342)	P value
Age (years)*	49 (46–52)	49 (46–52)	0.990
Male gender	137 (80.12)	274 (80.12)	1
Comorbidities			
Diabetes mellitus	32 (18.71)	27 (7.89)	0.001
Arterial hypertension	78 (45.61)	77 (22.51)	<0.001
Smoking	42 (28.97)	11 (3.22)	<0.001
Dyslipidemia	43 (25.29)	48 (14.04)	0.002
Obesity	98 (57.31)	27 (7.89)	<0.001
No information	39 (22.81)	296 (86.55)	
Family history of CHD	6 (3.51)	12 (3.51)	<0.001
No information	151 (88.30)	0	
Previous stroke	0	4 (1.17)	0.307
Peripheral vascular disease	2 (1.18)	2 (0.58)	0.603
Alcoholism	11 (6.43)	7 (2.05)	<0.001
No information	23 (13.45)	0	
Previous drug therapy			
Acetylsalicylic acid	65 (38.24)	32 (9.36)	<0.001
ACEI	25 (14.79)	23 (6.73)	0.006
ARB	36 (21.18)	35 (10.23)	0.001
Beta-blockers	38 (22.35)	25 (7.31)	<0.001

*Variables presented as median (interquartile range); ACEI: angiotensin converter enzyme inhibitor; ARB: angiotensin receptor blocker; CHD: coronary heart disease.

Table 2. Univariate logistic regression analysis of cardiovascular risk factors and coronary heart disease.

Variable	OR	95% CI	Interval	P value
Diabetes mellitus	2.915	1.615	5.261	<0.001
Arterial hypertension	2.752	1.852	4.089	<0.001
Dyslipidemia	2.104	1.319	3.358	0.002
Smoking	9.175	4.462	18.863	<0.001
Peripheral vascular disease	2	0.281	14.19	0.488
Alcoholism	3.44	1.266	9.39	0.015

OR: odds ratio; CI: confidence interval.

Table 3. Multivariate conditional logistic regression model of the association of traditional risk factors with CHD.

Variable	OR	95% CI	Interval	P value
Diabetes mellitus	2.043	0.11	4.58	0.083
Arterial hypertension	2.527	1.483	4.202	0.001
Smoking	7.15	3.196	15.996	<0.001

A retirement probability of 0.20 was used in the regression model. OR: odds ratio; CI: confidence interval.

50, there was an association between smoking and high blood pressure with CHD, but not for diabetes mellitus (OR, 10.39, 95% CI, 3.40–31.75, $p \leq 0.001$; OR, 2.37, 95% CI, 1.13–4.99, $p = 0.022$; and OR, 0.55, 95% CI, 0.17–1.77, $p = 0.32$, respectively). Individuals younger than 55 years who manifested a traditional risk factor (hypertension,

diabetes mellitus, smoking, or family history of CHD) increased CHD odds by 4.51 (95% CI, 2.92–6.96; $p \leq 0.001$).

Discussion

Traditional cardiovascular risk factors in the young adult population increase CHD risk. Coronary events occurring in this population are usually related to atherosclerosis, and the presence of one or more traditional risk factors associated with CHD has been reported.¹⁷ Although a smaller proportion of these risk factors have been presented in literature compared with populations older than 55 years, the prevalence is higher in individuals of the same age.^{18,19} In our study, two in three cases under 55 years old had at least one traditional cardiovascular risk factor not accounting for gender. The most frequent were hypertension (45.62%) and smoking (28.97%). Dyslipidemia (25.29%) and diabetes mellitus (18.7%) occurred less frequently.

However, this prevalence tends to be higher.^{6,20,21} In a retrospective cohort, Yandrapalli et al.⁶ describes a 27.4% prevalence of diabetes mellitus being higher in the Hispanic population. The reasons for the lower prevalence of diabetes mellitus are not clear. However, dyslipidemia, hypertension, obesity, and smoking proportion were also lower in our cases, which indicate that the people in our study manifested fewer traditional risk factors. Although more than one million patients were evaluated in the Yandrapalli study, they only analyzed temporal trends but did not look for an association between CHD and traditional risk factors in young

people.⁶ In contrast, Higuera et al.,²⁰ in a cross-sectional study of the Colombian population, reported a lower prevalence of diabetes mellitus, hypertension, dyslipidemia, and smoking compared to our study in patients aged between 18 and 50 years with an ACS. However, the study made by Higuera et al.²⁰ did not evaluate the association between CHD and traditional cardiovascular risk factors. In a retrospective cohort study in the Colombian population under 45 years of age with an ACS, Marin et al.²¹ reported a 66% and 64% prevalence of smoking and dyslipidemia, respectively, which is higher than our study population. However, arterial hypertension (28.2%) and diabetes mellitus (5.3%) in their study were less frequent than ours.²¹ Although their study was designed to describe the cases, they had no control group, which did not allow us to compare our results with the association of diabetes mellitus and other risk factors with CHD from their study.

The absence of a statistically significant association of diabetes mellitus in our multivariate regression model is to be noted. This was an unexpected finding, but it is in accordance with the study by von Eyben et al.,²² where there was no association between diabetes mellitus and CHD in patients under 41 years of age. However, the small number of patients involved and the retrospective nature of the study are precautions to be considered. In the INTERHEART study, which included Latin American population, diabetes mellitus doubled the chance of having an AMI in young individuals.²³ Also, the probability increased 1.6 times in individuals younger than 55 years, which is in contrast to our findings. Even though the limited sample size or the low prevalence of diabetes mellitus must be considered, it is also possible that the lack of association between diabetes and CHD in our study may be due to the less time of suffering from the disease.²³ If the patients in our population had suffered from diabetes mellitus for a shorter time, it is possible that this did not have enough time to affect the prognosis. Due to the design of this study, it is not possible to adjust for the duration of diabetes, and therefore, this explanation is speculative.

Our study suggests an association between traditional risk factors and CHD in people younger than 55 years old; however, this should not assume that young patient are exempted from presenting with an ACS. The data even suggest that the risk is higher if several risk factors are found in the same person.

The results of atypical risk factors found in this study should not be surprised since, in other classic and recent experiences, their low frequency has been described.^{24–28} Consumption of psychoactive substances, rheumatoid arthritis, Takayasu arteritis, chondrocalcinosis, and HIV were identified as risk factors in very few patients in our study.

The main limitations were the measurement of traditional cardiovascular risk factors based on medical records. There was a sub report of the obesity information, mainly in the controls. The same occurred for the magnitude of exposure to smoking and family history of CHD. The latter had an absence of information up to 80% of the cases. This may

explain the non-association of the family history in CHD risk, as well as the exclusion of statistical analysis of this variable and obesity. The limitations of our study design explain the absence of association of dyslipidemia in the multivariate analysis, since we did not have lipid profile results to determine the type of lipid metabolism disorder, and we lack information on obesity, a disorder that can influence the association of dyslipidemia and CHD. We did not observe an interaction between diabetes mellitus, smoking, or hypertension with dyslipidemia that could alter this relationship.

In addition, in this study, only patients with ACS who required PCI were evaluated. Young adults with CHD with an indication of surgical revascularisation or those with non-revascularised CHD due to bad distal beds or nonsignificant lesions were not included. Another limitation is the variation of the definition of a young adult in the studies, which makes the comparability of our results difficult. In our study, 5.2% of the individuals were under 40 years old and 76.61% were between 45 and 54 years old.

The strength of this study was the collection method of controls. It was done to control confusion factors, such as age, gender, temporal variability of ACS, and, in some degree socioeconomic strata pairing patients by age, gender, date of admission, and health insurance to the case. This strategy allowed us to make the controls, as much as possible, comparable at least in these factors. This is the only case-control study in young patients with AMI in the Colombian population where the traditional cardiovascular risk factors are explored, considering that it has an important internal validity.

Conclusion

The findings suggest that individuals younger than 55 years with traditional cardiovascular risk factors, such as hypertension and smoking, alone or in combination, have increased odds of CHD compared to patients of the same age, sex, and health insurance accessibility. Future studies are required to verify these findings.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The authors would like to thank Enago (www.enago.com) for the English language review. Acknowledgement of grant support: Fundación Valle del Lili.

Ethical approval

Ethical approval for this study was obtained from Clinical Research Center, Fundación Valle del Lili. acta No 16 del 11 de agosto de 2017).

Informed consent

Informed consent was not sought for this study because the study was retrospective, and no interventions or interviews were performed on patients.

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Supplemental material

Supplemental material for this article is available online.

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