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Original article

Factors associated with the risk of myocardial infarction in patients with type 2 diabetes mellitus

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ABSTRACT

Myocardial infarction is more frequent and has a worse prognosis in people with type 2 diabetes mellitus than in the general population. In order to identify factors associated with the risk of myocardial infarction in patients with type 2 diabetes mellitus, a case-control analytical study was conducted in 234 patients treated at the Endocrinology and Cardiology services of the Carlos Manuel de Céspedes hospital in the province of Granma, from January 1, 2018 to December 31, 2022. Classical and non-classical cardiovascular risk factors were evaluated, as well as some diabetes-specific conditions. Statistical tests: Chi-square and Student's t-test. Multivariate analysis showed five factors with independent influence on the development of myocardial infarction: microalbuminuria (OR= 21.09, CI= 3.0-148.0, p = 0.002); arterial hypertension (OR= 7.40, CI= 1.4-37.5, p = 0.016); age ≥ 60 years (OR= 6.72, CI= 1.0-44.9, p = 0.049); diabetes duration ≥10 years (OR= 4.07, CI=1.3-11.8, p =

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0.010); and low HDL cholesterol (OR= 3.21, CI=1.01-10.1, p = 0.046). The Hosmer-Lemeshow test demonstrated that the data fit the model (p = 0.914). A model was obtained demonstrating the independent influence of microalbuminuria, arterial hypertension, age, diabetes duration, and decreased HDL cholesterol on the development of myocardial infarction in people with type 2 diabetes mellitus.

Keywords: Risk factors; Myocardial infarction; Type 2 diabetes mellitus.

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Introduction

Myocardial infarction (MI), defined as the presence of acute myocardial damage detected by elevated cardiac biomarkers in the context of evidence of acute myocardial ischemia, is more frequent in patients with type 2 diabetes mellitus (DM) than in the general population. (1)In this sense, orA study conducted in Finland revealed that patients with type 2 diabetes without prior myocardial infarction (MI) were exposed to a risk of MI within 7 years comparable to that of non-diabetics with a history of MI. (2)

Furthermore, myocardial infarction (MI) has a worse prognosis in people with diabetes. Several studies in patients with unstable angina and MI demonstrate that individuals with diabetes mellitus (DM) had significantly increased adjusted relative risks with respect to all-cause mortality, death from cardiovascular disease, new MI, stroke, and new congestive heart failure. (3,4)

In this context, diabetes mellitus (DM) is considered a coronary risk equivalent. However, there is evidence of a wide distribution of myocardial infarction (MI) risk in patients with type 2 DM, depending, among other factors, on glycemic control, duration of the disease, and the amount of risk attributable to other concomitant factors. Therefore, most scientific societies recommend individualized cardiovascular risk assessment in people with DM. (5)

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The concept of risk factors for ischemic heart disease was first coined by the Framingham Heart Study. (6) This research demonstrated the epidemiological relationships between smoking, blood pressure, and cholesterol levels with the incidence of coronary heart disease. Since then, cohort studies have continued to explore the impact of different factors on the development of this disease.

Along these same lines, the present research aims to identify the factors associated with the risk of myocardial infarction in a group of people with type 2 DM.

Methods

An analytical case-control study was conducted on patients with type 2 DM, treated in the Endocrinology and Cardiology services of the Carlos Manuel de Céspedes provincial general hospital in the municipality of Bayamo, Granma province, from January 1, 2020 to December 31, 2024. Patients aged 40 years or older at the time of diabetes diagnosis were included, while those with MI in the course of a left bundle branch block and with diseases that could cause non-atherothrombotic MI were excluded.

The cases were represented by patients diagnosed with type 2 diabetes mellitus (DM2) who suffered myocardial infarction (MI), according to the criteria proposed by the American Diabetes Association Expert Committee. (7) The controls consisted of patients diagnosed with type 2 DM2 without MI. The criteria of the fourth universal definition were used for the diagnosis of MI. (1) Given that cardiac biomarkers are not available at the institution, the diagnosis was made based on clinical criteria (symptoms of acute myocardial ischemia), electrocardiographic criteria (new ischemic changes), and echocardiographic criteria (loss of viable myocardium).

The sample size was calculated using the EPIDAT statistical package version 4.2, and participants were selected by simple random sampling. A total of 234 patients were obtained, of whom 78 were cases and 156 were controls.

Techniques and procedures in obtaining information

The information was obtained from medical records. The following risk factors were evaluated: age, sex, family history of premature coronary artery disease, smoking, sedentary lifestyle, obesity,

hypertension, abdominal obesity, total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C), and microalbuminuria. Additionally, some diabetes-related conditions were considered, such as disease duration and glycemic control (glycated hemoglobin).

A family history of premature coronary artery disease was defined as myocardial infarction or sudden death before age 55 in male first-degree relatives or before age 65 in female first-degree relatives. A person was considered a smoker if they consumed cigarettes daily or almost daily, regardless of the number smoked, or if they reported quitting smoking six months prior to enrollment in this study. Any individual with low physical activity, as determined by the International Physical Activity Questionnaire, was considered sedentary. (8) Any patient receiving antihypertensive medication was considered hypertensive, regardless of blood pressure readings, or if systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg was recorded on two or more occasions. (9)

To assess nutritional status, the body mass index (BMI) was used, calculated using the following formula: weight (kg)/height (m2). A patient was classified as obese when the BMI was ≥ 30. Abdominal obesity was considered when the waist circumference was ≥ 102 cm in men and ≥ 88 cm in women. (10)

The cut-off points used to transform each of the quantitative variables into dichotomous variables, for their subsequent use in bivariate and multivariate analysis, were estimated according to the optimal cut-off point or minimum p-value method. In this way, the following cut-off points were established that defined those exposed to the following values: age ≥ 60 years, duration of DM ≥ 10 years, glycosylated hemoglobin (HbA1c) ≥ 10%, cholesterol ≥ 5.2 mmol/L, triglycerides ≥ 1.9 mmol/L, HDL-cholesterol ≤ 1.75 mmol/L, and microalbuminuria ≥ 30 mg/g.

Statistical analysis

Frequency distributions (absolute numbers and percentages) were obtained for qualitative variables, and the mean and standard deviation were calculated for quantitative variables. The chi-square test was used to examine the relationship between qualitative variables, and Student's t-test was used to compare the mean values of quantitative variables. A significance level (p) < 0.05 was assumed for all analyses.

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A bivariate and a multivariate strategy were used to analyze risk factors. The bivariate strategy was based on estimating risk using the odds ratio (OR), while the multivariate strategy assessed the independent influence of each variable on the probability of developing myocardial infarction (MI), while controlling for all other variables. The Hosmer-Lemeshow chi-square goodness-of-fit test was also applied. The SPSS 25.0 statistical package for Windows was used for all data analysis.

Ethical regulations

In carrying out this study, the ethical principles recommended in the Declaration of Helsinki for conducting research in the clinical-epidemiological field were taken into consideration.

Results

The overall characteristics of the sample are presented in Tables 1 and 2. Of the 234 patients studied, 119 (50.9%) were female and 115 (49.1%) were male. The mean age of the patients was 57.5 years, and the average duration of diabetes was 10.3 years. The most frequent comorbidities were hypertension (77.3%) and abdominal obesity (68.4%).

Table 1. Global characterization of the sample. Qualitative variables n = 234.

Variables	Category	Number	%
Sex	Male	115	49.1
	Female	119	50.9
Family history of premature coronary artery disease	Yeah	43	18.4
	No	191	81.6
Smoking	Yeah	28	11.9
	No	206	88.1
Sedentary lifestyle	Yeah	104	44.4
	No	130	55.6
High blood pressure	Yeah	181	77.3
	No	53	22.7
Obesity	Yeah	104	44.4
	No	130	55.6
Abdominal obesity	Yeah	160	68.4

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	No	74	31.6

Table 2. Global characterization of the sample. Quantitative variables n = 234.

Variables	Minimum	Maximum	Average	Standard deviation	Median
Age	35	89	57.56	11.18	59.0
Diabetes time	1	44	10.32	8.52	7.0
Systolic blood pressure	100	220	125.3	18.43	120
Diastolic blood pressure	60	110	79.61	9.88	80
Glycosylated hemoglobin	4.9	23.4	9.10	3.33	9.6
Total Cholesterol	2.9	12.0	4.51	1.27	4.7
Triglycerides	0.37	13.2	2.00	1.58	1.57
c-HDL	0.4	3.83	1.62	0.56	1.61
Microalbuminuria	3.21	136.5	29.78	27.27	19.68

c-HDL: high-density lipoprotein cholesterol.

Table 3 shows that 8 of the 14 factors evaluated significantly increased the risk of developing MI. Only a family history of premature coronary artery disease (p=0.191), triglycerides (p=0.194), sedentary lifestyle (p=0.353), male sex (p=0.643), obesity (p=0.016), and abdominal obesity (p=0.842) did not show a relevant relationship with the development of MI.

Table 3. Results of the bivariate analysis of cardiovascular risk factors and some conditions specific to diabetes mellitus.

Risk factors	Cases detected	Cases with IM Number (%)	OR	IC (95%)	Worth p
High blood pressure	181	75 (41.4)	11.79	3.54-39.23	0.000
Microalbuminuria	75	52 (22,2)	9.28	2.63-32.69	0.000
Age ≥ 60 years	185	73 (39.4)	5.73	2.17-15.14	0.001
Hypercholesterolemia	69	36 (52.2)	3.19	1.77-5.75	0.000
low c-HDL	140	60 (42.8)	3.16	1.71-5.84	0.000
Smoking	28	16 (57,1)	3.09	1.38-6.93	0.006
Family history of ECP	43	18 (41.8)	1.57	0.79-3.09	0.191
Hypertriglyceridemia	106	40 (37.7)	1.43	0.83-2.47	0.194
Sedentary lifestyle	104	38 (36.5)	1.29	0.75-2.23	0.353
Male	115	40 (34.8)	1.13	0.65-1.95	0.643
Abdominal obesity	160	54 (33.7)	1.06	0.59-1.90	0.842
Obesity	104	26 (25.0)	0.50	0.28-0.88	0.016

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Conditions specific to diabetes					
Diabetes duration ≥10 years	100	54 (54.0)	5.38	2.97-9.71	0.000
Glycemic dysregulation	190	67 (35.3)	2.81	1.05-7.48	0.039
Total population	234	78(33,3)	1.00		

CI: confidence interval; OR: odds ratio; c-HDL: high-density lipoprotein cholesterol; PCD: premature coronary artery disease

Multivariate analysis (Table 4) showed five factors with independent influence on the development of MI, which were: microalbuminuria (OR= 21.09, CI= 3.0-148.0, p = 0.002); arterial hypertension (OR= 7.40,IC= 1.4-37.5,p = 0.016); age (OR= 6.72,IC= 1.0-44.9,p = 0.049); the duration of diabetes (OR= 4.07,IC=1.3-11.8,p = 0.010) and low c-HDL (OR= 3.21,IC=1.01-10.1,p = 0.046).

Table 4. Multivariate analysis of cardiovascular risk factors.

Risk factors	β	Wald	OR tight	CI (95%)		p
				Lower	Superior	
Microalbuminuria	3,049	9,407	21.09	3.00	148.02	0.002
High blood pressure	2002	5,834	7,405	1,459	37,593	0.016
Age ≥ 60 years	1,905	3,863	6,722	1,005	44,949	0.049
Diabetes duration ≥10 years	1,405	6,626	4,074	1,398	11,873	0.010
low c-HDL	1,166	3,969	3,210	1,019	10.10	0.046

Hosmer and Lemeshow test p = 0.914

CI: confidence interval; OR: odds ratio; c-HDL: high-density lipoprotein cholesterol.

Discussion

The results of this research demonstrate that estimating the risk of myocardial infarction (MI) in people with type 2 diabetes (T2D) requires more than just classic cardiovascular risk factors; it is also necessary to consider non-traditional factors, as well as certain conditions specific to diabetes. Among these latter factors, the duration of diabetes stands out, as it has been shown to be an independent risk factor for MI. Exposure to chronic hyperglycemia may be the link between the

duration of the disease and the risk of macrovascular complications. However, it should be noted that in type 2 diabetes, complications can appear from the time of diagnosis.

Similar results to those of the present investigation were found in the DISCOVER study program, (11) conducted with 15,992 patients with type 2 diabetes. The authors found that the duration of diabetes was significantly associated with macrovascular complications (RR = 1.02, 95% CI = 1.01–1.02). Likewise, Nanayakkara N et al. (12), in a study that included 3,419 adults with type 2 diabetes in Australia, confirmed that the duration of diabetes was independently associated with macrovascular complications ($p < 0.001$).

The data from this study confirm that microalbuminuria is an independent predictor of myocardial infarction (MI) in people with type 2 diabetes. The link between microalbuminuria and MI may lie in endothelial dysfunction. In diabetes, chronic hyperglycemia compromises the integrity of the glomerular filtration barrier, which is composed of glomerular endothelial cells; therefore, microalbuminuria reflects extensive vascular damage throughout the body and is considered a marker of endothelial dysfunction. (13)

In line with the results of the present study, the Empagliflozin Cardiovascular Outcome Event Trial, (14) conducted in patients with type 2 DM, demonstrated that a 30% decrease in urinary albumin excretion significantly reduced the risk of major cardiovascular events (HR = 0.96; 95% CI = 0.93–0.99; p=0.012), cardiovascular deaths and hospitalizations for heart failure (HR = 0.94; 95% CI = 0.91–0.98; p = 0.003).

Hypertension in people with diabetes has characteristics that accelerate coronary artery disease, justifying the results of this research. Specifically, the systolic component predominates, making it more difficult to treat and control; there is a lack of nocturnal blood pressure reduction during sleep (non-dipper pattern); and there is premature target organ damage. (15)

A systematic review and meta-analysis that evaluated 16 randomized controlled trials in patients with type 2 diabetes, conducted by Wang J et al. (16), found results similar to those of the present study. These authors found that intensive blood pressure-lowering treatment significantly reduced the risk of major cardiovascular events (RR = 0.82; 95% CI = 0.73–0.92), myocardial infarction (RR = 0.86; 95%

CI = 0.77–0.96), stroke (RR = 0.72; 95% CI = 0.60–0.88), and cardiovascular death (RR = 0.73; 95% CI = 0.58–0.92), compared with less intensive treatment.

Predictive scales created from cohorts of people with diabetes have shown, as has the present work, that age is a strong predictor of MI, (17) although the existing age thresholds for identifying people with diabetes who are at high risk of MI are not well known.

The Global Burden of Disease Study (18) found that the incidence of myocardial infarction (MI) worldwide in 2019 increased from the fourth decade of life onward and did not decrease thereafter. The results of the present study are in line with this. It is important to note that the mean age of the sample was high, which may have influenced this result and the high age cutoff point at which healthy and diseased individuals could be better differentiated (57.5 years).

The results of this research are consistent with decades of research that have shown that low plasma levels of c-HDL are associated with an increased risk of coronary heart disease.From a pathophysiological point of view, this relationship is explained by the fact that c-HDL exerts a series of anti-atherogenic functions such as mediating the efflux of cholesterol from foam cells of macrophages, reverse transport of cholesterol to the liver, direct stimulation of endothelial nitric oxide production, and inhibition of lipid oxidation. (19)

However, the causal role of HDL-C in the pathogenesis of atherosclerosis, as well as its potential as a therapeutic target, is currently being examined by Mendelian randomization data showing that HDL-C may not be a cause of cardiovascular disease. Furthermore, drugs that increase HDL-C have largely failed to prevent or treat cardiovascular disease. (20)

The present study concludes that the factors with the greatest influence on the development of myocardial infarction in patients with type 2 DM are microalbuminuria, high blood pressure, age, a diabetes duration greater than 10 years, and decreased HDL-C.

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Conflicts of interest

The authors declare no conflicts of interest.

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Authorship contribution

Eduardo René Valdés Ramos: conceptualization, data curation, formal analysis, research, writing of the original draft.

Alexis Álvarez Aliaga: methodology, supervision and validation, drafting of the original draft.

Eduardo Valdés Bencosme: resources, writing, revision and editing.