Cardiovascular risk factors associated with coronary ectasia and acute myocardial infarction

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Abstract

Introduction: Coronary ectasia has a low prevalence in the general population. Its risk factors may differ from those of coronary artery disease. **Objective:** To identify the prevalence of coronary ectasia in patients with acute myocardial infarction (AMI) and cardiovascular risk factors (CVRFs). **Methods:** Retrospective, cross-sectional study. Out of 3,254 cardiac catheterizations for AMI during one year, 2,975 had no coronary ectasia. We included 558 patients with coronary ectasia on coronary angiography and, as controls, subjects with similar characteristics except for coronary ectasia, and CVRFs were recorded. Descriptive statistics, bivariate and multivariate analysis were used; odds ratio (OR) was calculated. **Results:** 279 patients with and without coronary ectasia were studied. The prevalence of coronary ectasia was 8.5 %. The platelet/lymphocyte ratio (PLR) was higher in patients with ectasia than in those without ectasia ($p = 0.003$). In the bivariate analysis, associated CVRFs were overweight, obesity and diabetes, and in the multivariate analysis, hypercholesterolemia (OR: 3.90; $p = 0.0001$) and exposure to herbicides (OR: 6.82; $p = 0.020$). **Conclusions:** A high prevalence of coronary ectasia was found, with the main risk factors being a history of herbicide use and hypercholesterolemia. PLR was found to be elevated in these patients. Early detection is important due to its association with acute coronary events.

KEY WORDS: Coronary artery disease. Myocardial infarction. Prevalence. Herbicides. Angiography.

Factores de riesgo cardiovascular asociados a ectasia coronaria e infarto agudo de miocardio

Resumen

Introducción: La ectasia coronaria tiene baja prevalencia en población general, los factores de riesgo pueden diferir de la enfermedad arterial coronaria. **Objetivo:** Identificar la prevalencia de ectasia coronaria en pacientes con infarto agudo de miocardio (IAM) y factores de riesgo cardiovascular (FRCV). **Métodos:** Estudio retrospectivo, transversal. De 3,254 cateterismos cardíacos por IAM durante un año, 2,975 no presentaron ectasia coronaria. Se incluyeron 558 pacientes clasificados como portadores de ectasia coronaria en coronariografía y controles aquellos con características similares exceptuando la ectasia coronaria y se registraron los FRCV. Empleamos estadística descriptiva, análisis bivalente, multivalente y calculamos

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el odds ratio (OR). **Resultados:** Se estudiaron 279 pacientes con y sin ectasia coronaria. La prevalencia de ectasia coronaria fue del 8.5%. El índice plaqueta/linfocito (IPL) se encontró más elevado en pacientes con ectasia que en aquellos sin ectasia ($p = 0.003$). En el análisis bivalente los FRCV asociados fueron sobrepeso, obesidad y diabetes, y en el multivariante la hipercolesterolemia (OR: 3.90; $p = 0.0001$) y exposición a herbicidas (OR: 6.82; $p = 0.020$). **Conclusiones:** Encontramos alta prevalencia de ectasia coronaria, los principales factores de riesgo fueron el antecedente de uso de herbicidas e hipercolesterolemia. Identificamos el IPL elevado en estos pacientes. Es importante la detección oportuna debido a su asociación con eventos coronarios agudos.

PALABRAS CLAVE: Enfermedad coronaria. Infarto de miocardio. Prevalencia. Herbicidas. Angiografía.

Introduction

The term coronary artery ectasia (CAE), coined in 1966, is defined as coronary artery dilatation that exceeds adjacent segments normal diameter or the diameter of the largest coronary artery by at least 1.5 times^{1,2}.

Atherosclerosis is its main cause, with predominance in males, and association with traditional cardiovascular risk factors (CVRFs) in more than 50% of cases, with 30% being caused by congenital anomalies and the remaining 20% by autoimmune etiologies, connective tissue disease, infectious and post-traumatic causes, as well as use of herbicides and cocaine consumption. The right coronary artery is the most compromised (40-61%), followed by the anterior descending (15-32%) and left circumflex arteries (15-23%). In 75% of cases, ectasias are of single vessel. More than 80% of ectasias are associated with obstructive coronary artery disease³⁻⁵.

The largest study was carried out in China, where, among 42,800 cardiac catheterizations, a prevalence of CAE of 1.3% was reported, which was associated with the male gender, hypertension, smoking, dyslipidemia and only 27.5% had myocardial infarction. In Asian countries such as Singapore, India, Iran and Turkey, rates of prevalence of 1.2, 1.9, 2.3 and 4.2% were documented, with a history of myocardial infarction in 13-25% of the study populations⁶⁻⁹.

In Spain, a prevalence of CAE of 3.4% was reported in a total of 4,332 analyzed coronary angiograms, with 40.8% of CAE cases showing myocardial infarction¹⁰. The lowest prevalence worldwide was observed in a Swedish-Irish study, where among 16,454 angiograms, only 0.4% of cases of CAE was found, out of which in 62% was there a history of ischemic heart disease¹¹. The highest figure (6%) was documented in Saudi Arabia, where 1,115 catheterizations were analyzed¹².

In Mexico, there are only two publications on the subject, where catheterizations were analyzed at

tertiary care hospitals, with a prevalence of 2.3 and 4.5% being reported, out of which 22 and 84.6%, respectively, had myocardial infarction^{13,14}. In both studies there was no clear association of CVRFs with regard to that of other countries. The purpose of the study was to investigate the prevalence of coronary artery ectasia in patients with acute myocardial infarction and to analyze associated CVRFs.

Methods

The present study was carried out at the hemodynamics department and coronary care unit of a tertiary care hospital in Mexico City. The study design was observational, retrospective, case-control.

For the cases, patients with acute myocardial infarction, of either gender, older than 18 years of age, with a concomitant finding of CAE on coronary angiography were included. Patients with a diagnosis of unstable angina or stable chronic angina at discharge were not included. Patients for whom 80% of the information required for analysis was not obtained were excluded.

For the control group, patients diagnosed with acute myocardial infarction without CAE on coronary angiography, of both genders, older than 18 years of age, with non-inclusion and exclusion criteria similar to those for the cases, were included. For each patient with CAE, a control was included at a 1:1 ratio. Control group cases were randomly obtained among all coronary angiography procedures carried out within that period.

Methodology

The project was approved by the local research committee, with registration number R2018-3501-116. The reviewed medical charts were selected from the database and electronic medical records of the coronary care unit department, and corresponded to patients who were hospitalized in said services from July

Table 1. Cardiovascular risk factors in patients with and without coronary artery ectasia

Variable	Acute myocardial infarction without ectasia (n = 279)	Acute myocardial infarction with ectasia (n = 279)	p
Female gender	68 (24.4%)	35 (12.5%)	0.001*†
Male gender	211 (75.6%)	244 (87.5%)	0.001*†
Diabetes mellitus	141 (50.5%)	102 (36.6%)	0.001*†
Hypertension	193 (69.2%)	183 (65.6%)	0.367*
Smoking	158 (56.6%)	158 (56.6%)	1*
Hypercholesterolemia	64 (23.1%)	132 (47.3%)	0.001*†
Cocaine use	1 (0.4%)	1 (0.4%)	1*
Exposure to herbicides	2 (0.7%)	12 (4.3%)	0.007*†
Autoimmune diseases	5 (1.8%)	3 (1.1%)	0.476*
Obesity	55 (19.7%)	126 (45.2%)	0.001*†
Overweight	117 (42.2%)	161 (57.8%)	0.001*†

*Chi-square test.

†Statistically significant.

2018 to July 2019 and who underwent coronary angiography. Data were obtained for each patient, including name, age, gender, traditional CVRFs (smoking, obesity, overweight, history of hypercholesterolemia and hypertriglyceridemia, diabetes mellitus, hypertension) according to the medical history, non-traditional CVRFs (cocaine use, autoimmune diseases, connective tissue diseases such as Marfan syndrome or Ehlers Danlos syndrome, exposure to herbicides), as well as laboratory parameters upon admission to the coronary care unit, such as total lymphocyte count, hemoglobin, uric acid, leukocytes, polymorphonuclear leukocytes, platelets, neutrophil:lymphocyte ratio, platelet:lymphocyte ratio (PLR), red cell distribution width, creatine phosphokinase, creatine phosphokinase MB fraction, albumin, total cholesterol, low-density lipoprotein cholesterol (LDL-C) and triglycerides. All these parameters were recorded at coronary care unit admission.

Statistical analysis

Descriptive statistics were used with central tendency measures (mean, median), standard deviation, ranges, percentages; for the comparison of variables without normal distribution, Mann-Whitney's U-test was used. A bivariate logistic regression analysis was carried out to measure the effect of each factor on CAE, and a multivariate analysis with odds ratio (OR) was

used to evaluate which variable could be predictive of this entity as an independent risk factor, with a p-value < 0.05 being established as statistically significant. Statistical analysis was carried out using the SPSS program, version 25.0 (Chicago, Illinois), developed by International Business Machines Corporation (IBM).

Results

We analyzed a total of 558 cardiac catheterization procedures for acute myocardial infarction over a one-year period. Of these procedures, 279 involved patients with myocardial infarction without CAE and 279 with CAE. In the group with CAE, the male:female ratio was 2.5:1; in addition, 57.8% had overweight, 45.2% obesity, 36.6% were diabetes mellitus carriers and 4.3% had a history of exposure to herbicides (Table 1).

Of the 279 patients with CAE, 49.1% had Markis I ectasia (involvement of two or more vessels); 13.97%, Markis II ectasia (involvement of one vessel and a segment of another); 27.95%, Markis III ectasia (involvement of a single vessel); and 8.96%, Markis IV ectasia (involvement on a segment of a single vessel).

Median body mass index was higher in the ectasia group, while median platelets were lower. PLR was higher for the group with ectasia (p = 0.003) (Table 2).

On angiographic characterization, the right coronary artery was observed to be more compromised (35.1%),

Table 2. Demographic and paraclinical values in patients with and without coronary artery ectasia

Variable	Infarction without ectasia (n = 279)	Infarction with ectasia (n = 279)	p
Age, years	65 (56-71)	63 (56-71)	0.325*
Body mass index	24.6 (23-27.4)	28 (25.8-33.2)	0.0001**
Lymphocytes, μ L	1,368 (990-1,782)	1,376 (960-1,859)	0.959*
Hemoglobin, g/dL	14.1 (12.7-15.3)	15.2 (13.9-16.4)	0.0001**
Triglycerides, mg/dL	119 (88.25-158)	130 (99.5-178.5)	0.006**
Uric acid, mg/dL	5.75 (4.30-7.05)	5.70 (4.80-7.50)	0.604*
Leukocytes, μ L	9,700 (7,300-12,200)	9,300 (7,400-12,100)	0.641*
Polymorphonuclear leukocytes, μ L	7,128 (4,836-9,782)	6,720 (4,898-9,625)	0.416*
Platelets, μ L	252,000 (20,500-30,200)	217,000 (17,500-266,250)	0.000**
NLR	4.94 (0.46-36.59)	5.07 (0.21-64)	0.610*
PLR	160.16 (118.25-227.22)	177.79 (129.90-252.87)	0.003**
RDW	13.9 (13.4-14.4)	13.6 (13.2-14.2)	0.001**
CK, U/L	2,523 (1,876-3,621)	2,450 (1,836-3,557)	0.832*
CKMB, U/L	452 (390-543)	457 (391-621)	0.017**
LDL-C, mg/dL	104.4 (47-171)	88 (75.6-124.750)	1*
Cholesterol, mg/dL	131 (108-168.5)	148 (119-180.5)	0.005**
Albumin, g/dL	3.5 (3.1-3.8)	3.7 (3.3-4)	0.005**

*Mann-Whitney's U-test.

**Statistically significant.

NLR: neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio; RDW: red cell distribution width; CK: creatine phosphokinase; CKMB: creatine phosphokinase MB fraction; LDL-C: low-density lipoprotein cholesterol.

Table 3. Culprit vessel

	Acute myocardial infarction without ectasia (n = 279)	Acute myocardial infarction with ectasia (n = 279)
Right coronary artery	44 (15.8)	98 (35.1)
Circumflex artery	11 (3.9)	25 (9)
Anterior descending	0 (0)	81 (29)
Three-vessel disease	89 (31.9)	36 (12.9)
Two-vessel disease	74 (26.5)	39 (14)

followed by the anterior descending artery (29%); the least compromised artery was the circumflex (9%) (Table 3). Figure 1 illustrates a representative example of ectasia involving the right coronary artery.

In the bivariate analysis, diabetes mellitus, overweight and obesity were found to be factors associated with CAE (Table 4). In the multivariate analysis,

Figure 1. Right coronary artery ectasia. Image showing ectatic right coronary artery, with vertical segment thrombus image and TIMI 0 flow in a patient with Markis I coronary artery ectasia.

only hypercholesterolemia and exposure to herbicides conferred risk for developing CAE.

Table 4. Clinical variables in the logistic regression model for coronary artery ectasia

Variable	Bivariate analysis			Multivariate analysis		
	Risk	95% CI	p	OR	95% CI for OR	p
Diabetes mellitus	1.382	(1.1-1.6)	0.001*	0.412	(0.2-0.6)	0.0001
Overweight	1.730	(1.3-2.2)	0.0001*	0.171	(0.10-0.27)	0.0001
Obesity	1.983	(1.5-2.5)	0.0001*	0.135	(0.08-0.21)	0.0001
Hypercholesterolemia	0.492	(0.3-0.6)	0.0001	3.90	(2.5-5.9)	0.0001*
Exposure to herbicides	0.167	(0.03-0.7)	0.012	6.82	(1.34-34)	0.020*
Smoking	1	(0.8-1.1)	1	1.205	(0.8-1.7)	0.352
Hypertension	1.055	(0.9-1.1)	0.416	0.79	(0.52-1.1)	0.271

CI: confidence interval; OR: odds ratio.

*Statistically significant.

Discussion

We found a prevalence of coronary artery ectasia of 8.5%, which is one of the highest that has been documented in the world in the context of patients with acute myocardial infarction who underwent coronary angiography. There was a predominance in men, with 87.5%, in contrast to 12.5% in women with CAE, which corresponds to a 12:1 ratio, and which is consistent with results obtained in other retrospective studies^{1,4}.

In our research, the disease compromised more than two vessels in more than half the cases, which differs from the study carried out by Zhang⁵, where 72.4% of patients with CAE had involvement of a single vessel (Markis types III and IV).

Previous investigations have evaluated the presence of CAE from another perspective, either by incidence, prognosis, mortality or coexistence of coronary artery disease; however none of them focuses on patients with myocardial infarction⁶⁻⁷.

As risk factors associated with CAE, we found the presence of diabetes, overweight and obesity, and as independent risk factors, hypercholesterolemia and exposure to herbicides. Similar to our results, the study by Armirzadegan et al.⁸, carried out in Iranian population, found that overweight and obesity were more common and had a significant difference in patients with CAE in comparison with patients with coronary artery stenosis.

Hypercholesterolemia as an independent risk factor for CAE has variable results, with regard to the analyzed population. In a study carried out in patients from Sweden and Ireland by Boles et al.¹¹, although hyperlipidemia was more commonly found in patients with CAE,

the difference was not significant; in our study we found an association with hypercholesterolemia.

We found a prevalence of CAE of 8.5%, which is one of the highest documented in the world in the context of patients with acute myocardial infarction who underwent coronary angiography. This prevalence is higher than that described in Saudi Arabia of 6%, which has reported the highest rates of prevalence; however, only 57% of subjects had a history of myocardial infarction¹².

Hematological differences were found between both groups, as in the case of hemoglobin in patients with ectasia, which was slightly higher in comparison with those without ectasia. PLR is a prognostic and diagnostic marker in coronary artery disease, and elevated levels thereof are associated with an unfavorable prognosis in patients with acute coronary syndrome, given that this reveals changes in platelet and lymphocyte counts due to acute inflammatory and prothrombotic states. There is only one study carried out in this regard in the context of acute myocardial infarction and CAE, in Turkey, by Kundi et al.¹⁵, who found that patients with CAE had a significantly higher PLR, and it was regarded as a risk factor in comparison with patients with obstructive coronary disease. PLR values were also found to be elevated in our study; however, it was not longitudinally measured.

Red cell distribution width reflects the variability in circulating red blood cells size (anisocytosis), and has been associated with cardiovascular events due to inflammatory mechanisms and neuro-humoral activation, with a pathogenic role in atherosclerotic coronary artery disease having been identified. In a study carried out by Dogdu et al.¹⁶, where they evaluated a group of patients with CAE and other control group

without ectasia, the levels of red cell distribution width (RDW) were found to be significantly higher in the group with CAE in comparison with the control group. Conversely, in our study, a slightly higher level of RDW was found in the group without CAE.

Finally, exposure to herbicides had a larger weight on ectasia accompanying infarction. The components that are most common to herbicides are 2,4,5-T (trichlorophenoxyacetic acid), 2,4 D (dichlorophenoxyacetic acid) or a cholinesterase inhibitor. Chronic exposure to these agents can elevate acetylcholine levels in a focal region of the coronary interstitium through competitive inhibition and thus increase acetylcholine end-products, which are potent stimulators of nitric oxide, an endothelium-derived relaxation factor¹⁷. In Mexico, as in other countries, the use of herbicides continues despite their deleterious effects on the environment and toxicity, including its association with CAE.

Some limitations of the study should be taken into account. Due to its cross-sectional design, patients did not undergo follow-up. PLR was only measured once, and thus its prognostic value is unknown. Another limitation is tertiary care reference bias, as well as the fact that the type of herbicide and the route and time of exposure were not specified; in addition, other risk factors such as hyperhomocysteinemia, among others, were not evaluated¹⁸.

We consider that the results of this study are relevant due to the high prevalence of CAE that was found in this population with myocardial infarction. A recent study carried out in China found that, out of 11,267 angiograms that were performed in patients with suspected coronary artery disease, only 1% corresponded to CAE¹⁹.

Conclusions

A high prevalence of coronary artery ectasia was found in patients with myocardial infarction, with main risk factors being hypercholesterolemia and exposure to herbicides. PLR was found to be elevated in patients with CAE, with this being a reflection of the inflammatory process. Timely detection of this entity is important given its association with acute coronary events. Prospective studies assessing long-term prognosis of these patients are required.

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Conflict of interests

None of the authors has conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this research.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained informed consent from the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

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