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X syndrome of coronary microcirculation, coronary spasms and acute myocardial infarction in patients without significant coronary lesions

Síndrome X de microcirculación coronaria, espasmo coronario e infarto agudo de miocardio en pacientes sin lesiones coronarias significativas

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To the Editor,

For many years, there has been talk of Syndrome X X syndrome of coronary microcirculation and coronary artery spasm[1,2]. However, a phenomenon of such magnitude is frequently played down when a patient with acute myocardial infarction (AMI) presents with normal coronary angiography[3]. In fact, many cardiologists are reluctant to meet the uncertainty of an ongoing unresolved cause, especially those who work in hospitals lacking more sophisticated studies to define a major issue for any doctor: the cause of the problem.

Although the possibility of coronary spasm may be considered after a normal coronary angiography, investigations to demonstrate it are not carried out due to the risk/benefit ratio or lack of necessary resources.

For these reasons, the clinical cardiologist, or any other specialist dedicated to cardiovascular diseases, faces an enigma where the response may have some scientific level, but almost always theoretical and unconvincing. In short, it is often impossible to obtain an exact and final explanation of the problem in the case of AMI with normal coronary arteries[4].

There are different studies, not available in all health institutions, that help to clarify it and stratify the patient's risk, although, in isolation, they are also not finally convincing to explain the cardiovascular phenomenon in question, but they are very useful when their results are combined[5]. Among them are[5-8]: Ergometry, stress (physical or pharmacological) echocardiography, as well as contrast and tissue characterization echocardiography, nuclear medicine studies (myocardial perfusion scintigraphy with single photon emission-computed tomography

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[SPECT]), computed axial tomography, and magnetic resonance imaging, which offers advantages in relation to the remaining non-invasive imaging techniques for the diagnosis of microvascular dysfunction[8].

For these reasons, a retrospective descriptive study was conducted to determine the association of some clinical-epidemiological variables in 192 patients with AMI and normal coronary arteries, assisted at the Department of Cardiology in the "Hospital Provincial Docente Roberto Rodríguez" in Morón, Ciego de Ávila, Cuba, from January 2016 to December 2017.

This hospital does not have a Department of Interventional Cardiology; therefore, every coronary angiography was performed at the "Cardiocentro Ernesto Che Guevara" of Santa Clara, the "Instituto de Cardiología y Cirugía Cardiovascular" of Havana, and the "Hospital Hermanos Ameijeiras" also in the capital of the country.

All patients had coronary angiography results without lesions or significant lesions (<50% of artery lumen occlusion).

The main epidemiological variables analyzed were: smoking habit, overweight, obesity, alcoholism, and personal pathological history of diabetes mellitus, dyslipidemia, high blood pressure, dietary habits, salt intake and physical activity.

The **table** shows the distribution of patients according to sex and age groups demonstrating a predominance in male (58.33%), age groups between 45-54 years (37.5%), and from 55 years and up (42.71%).

All patients with normal coronary angiography (192 patients) had a smoking habit with more than 15 years of progression (**Figure**), which was more noticeable in men. Dyslipidemia (72.6%) was also more frequent in them, but only up to 50 years, as it predominated in women from over that age. There was a high prevalence of diabetes mellitus (21% insulin-dependent and 61.5% non-insulin-dependent). All had poor dietary habits, ate too much salt and did not exercised on a regular basis. However, regardless of these associations, the investigation did not confirm a significant correlation between syndrome X microvascular due to microvascular dysfunction, coronary spasm and AMI with normal coronary arteries.

Coronary artery disease (CAD) may be obstructive or not, according to the presence or absence of coronary lesions and their severity[9]. Years ago it was believed that having a non-obstructive CAD represented a relatively benign prognosis, but it has already been shown that these patients are more likely to have adverse cardiac events than the healthy population[1,10,11]. The diagnosis of X syndrome is often by exclusion but it requires invasive tests to demonstrate the absence of significant stenosis in the epicardial coronary arteries or coronary vasospasm[1]. However, focusing the diagnosis in the search for the possible causes of ischemia requires a more detailed analysis than simply considering the anatomical state of the coronary arteries, which is why studies enabling a functional assessment such as coronary flow reserve among others have also emerged[12].

In women's X syndrome there are: chest pain, myocardial ischemia during exercise stress test, and absence of obstructive CAD[13]. A stricter definition includes: stress-induced angina, ST-segment depression during the anginal episode, normal epicardial coronary arteries or with no significant lesions, absence of spontaneous or induced coronary vasospasm in the provocation test with ergonovine or

Table. Distribution of patients according to sex and age groups. "Hospital General Docente Roberto Rodríguez Fernández". Morón, Ciego de Ávila, Cuba.

Age groups (Years)	Female		Male		Total	
	Nº	%	Nº	%	Nº	%
Less than 35	2	1.04	4	2.08	6	3.12
35 – 44	10	5.21	22	11.46	32	16.67
45 – 54	26	13.54	46	23.96	72	37.50
55 and up	42	21.88	40	20.83	82	42.71
Total	80	41.67	112	58.33	192	100

Source: Patients' record, Department of Cardiology.

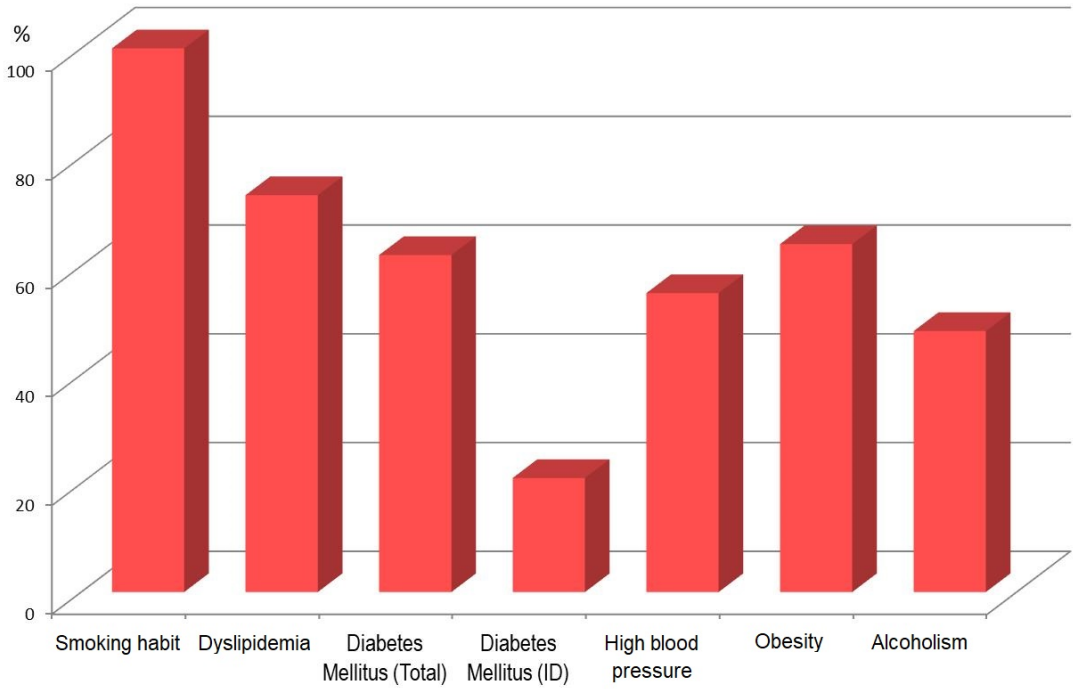

Figure. Distribution of risk factors. ID, insulin-dependent.

acetylcholine, and absence of cardiac or systemic diseases associated with microvascular dysfunction, such as hypertrophic cardiomyopathy and diabetes mellitus[14].

Its pathogenesis remains unclear, but several mechanisms have been suggested[2,15-18], among them are: alteration in the regulation of coronary microcirculation due to autonomic disorders and mechanisms of endothelial dysfunction, generalized vascular alterations, subendocardial perfusion abnormalities, inflammation, hyperinsulinemia, hormonal deficit (polycystic ovarian syndrome, hypoestrogenemia, menopause) and abnormal perception of pain.

AMI with normal coronary arteries is a controversial issue. Despite everything we know, much remains to be studied and clarified in order to truly define the genesis or cause of this problem. Moreover, it should receive as much attention as any well-known coronary disease, so in the case of these patients, all preventive and therapeutic measures must be taken with precision and seriousness. In this sense it is important to point out that Jespersen *et al*[10] found that non-obstructive CAD in patients referred to coronary angiography due to suspected ischemic heart disease was much more frequent in women than in men (65% vs. 30%), and concluded that patients with stable angina and normal coronary arteries or without significant lesions have a high risk of serious cardiovascular events and all-cause mortality, compared to a reference population without ischemic heart disease.

CONFLICT OF INTERESTS

None

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