INTERVENTIONAL CARDIOLOGY

Coronary Ectasia: Prevalence, and Clinical and Angiographic Characteristics

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Introduction and objectives. Coronary ectasia is characterized by the presence of diffuse dilation of the coronary vessels and is detected in 0.3-5.3% of angiographic studies. Our objective was to evaluate the prevalence of this condition, to analyze its clinical and angiographic characteristics, and to compare patients with ectasia and patients without it.

Patients and method. Coronary angiography was performed in 4.332 patients from October 1998 to June 2001. This population was divided in two groups, patients with and patients without ectasia and patients without ectasia. Angiographic and clinical variables were compared in these groups.

Results. The prevalence of ectasia was 3.39%. Most patients with ectasia (77.6%) had coronary stenosis. Ectasia affected a single vessel in 49.7%, most frequently the right coronary artery (132 patients), which also showed the greatest dilation. Most patients with ectasia were men (91.2%), smokers (56.5%), and younger than patients without ectasia (60.8 ± 11.7 vs. 63.3 ± 10.7 years; *P* = 0.01). They also had a lower prevalence of diabetes (22.4%) and previous revascularization procedures (8.2% angioplasty and 1.4% surgical revascularization).

Logistical regression analysis showed that only male sex was associated to the presence of ectasia (OR = 3.33; 95% CI, 1.81-6.13) and that only diabetes was independently associated with absence of ectasia (OR = 0.65; 95% CI, 0.43-0.98).

Conclusions. The prevalence of coronary ectasia in patients who underwent angiography was 3.4%. Coronary ectasia was prevalent in males and associated to the classic cardiovascular risk factors, except diabetes, a pathology that was less frequent than usual.

Key words: *Coronary artery disease. Angiography. Atherosclerosis. Aneurysm. Diabetes mellitus.*

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Ectasia coronaria: prevalencia, características clínicas y angiográficas

Introducción y objetivos. La ectasia coronaria constituye una dilatación difusa del vaso, que aparece en el 0,3-5,3% de las coronariografías. El objetivo de este artículo es conocer su prevalencia en nuestro medio, analizando sus características y comparándolas con las de la población sin ectasia.

Pacientes y método. Desde octubre de 1998, los pacientes remitidos al laboratorio de hemodinámica para coronariografía que presentan coronarias ectásicas son incluidos en un registro prospectivo. Se analizan las distintas variables clínicas y angiográficas de los pacientes con y sin ectasia coronaria.

Resultados. La prevalencia de ectasia fue del 3,39%. Un 77,6% presentaba estenosis coronarias significativas. Afectaba a un solo vaso en el 49,7%, siendo la coronaria derecha (n = 132) la más frecuentemente afectada y la que presentaba un mayor grado de dilatación. La mayoría de los sujetos con ectasia fueron varones (91,2%), fumadores (56,5%), más jóvenes que los pacientes sin ectasia (60,8 ± 11,7 frente a 63,3 ± 10,7 años; p = 0,01), y con menor prevalencia de diabetes (22,4%) y antecedentes de revascularización (8,2% angioplastia y 1,4% cirugía).

En el modelo de regresión logística, el sexo masculino fue la única variable asociada a la presencia de ectasia (OR = 3,33; IC del 95%, 1,81-6,13), mientras que la diabetes se asoció de forma independiente con la ausencia de coronarias ectásicas (OR = 0,65; IC del 95%, 0,43-0,98).

Conclusiones. La prevalencia de ectasia coronaria entre los pacientes sometidos a coronariografía por sospecha de cardiopatía isquémica es del 3,4%. Predomina en los varones y se asocia a los clásicos factores de riesgo, con excepción de la diabetes, una enfermedad que aparece con menor frecuencia de lo habitual.

Palabras clave: *Enfermedad coronaria. Angiografía. Aterosclerosis. Aneurisma. Diabetes mellitus.*

INTRODUCTION

Coronary artery ectasia (CE) is defined as a ≥1.5-fold dilation with respect to the diameter of adjacent normal segments of the same or other arteries.[1] A dif-

ABBREVIATIONS

RCA: right coronary artery
CX: circumflex artery
ADA: anterior descending artery
CE: coronary artery ectasia
HT: hypertension
TIMI flow: classification of blood flow according to TIMI (Thrombolysis in Myocardial Infarction) system

fuse condition, it must be distinguished from discrete aneurysms or localized dilations that appear in areas adjacent to coronary artery stenosis in some cases of Kawasaki disease[2] and other conditions.

Prevalence of CE varies between 0.3% and 5.3% depending on series, but appears to have increased in recent years.[3-5] The cause of CE has been linked to various agents such as exposure to herbicides,[6] Takayasu aortitis,[7] polyarteritis nodosa,[8] vascular trauma or lesions.[9] In most cases it seems to be related to coronary arteriosclerosis.[10] Most commonly, patients present with associated coronary artery stenosis, even in cases when lesions to coronary arteries are absent. Patients suffer angina, vasospasm[6] and myocardial infarction.[8-11] The real prevalence in our setting is unknown, as are its clinical presentation and evolution.

Our objectives are:

– To study the prevalence of CE in the population of patients referred to our hemodynamics laboratory for coronary angiography.

– To describe clinical characteristics of patients with CE, analyzing presentation and cardiovascular risk.

– To study angiographic characteristics of patients with CE.

– To compare clinical and angiographic variables in patients with and without CE.

PATIENTS AND METHOD

This was a cross-sectional study of patients undergoing coronary angiography and presenting with some degree of CE between October 1998 and June 2001. Patients with valvular heart disease, cardiomyopathy or congenital heart problems were excluded as CE could develop as a secondary consequence of these conditions.

From October 1998, patients with CE were identified and followed clinically with twice-yearly checkups. Coronary artery ectasia was defined as a dilation of the coronary artery longer than 20 mm and a ≥1.5-fold in diameter when compared to the adjacent normal segment. The hemodynamic specialist and one of the physicians in charge of the study agreed on an estimated "normal" caliber when no such segment existed (Figure 1). Similarly, patients were included in the study as a result of a joint decision. After visual assessment, quantitative information was obtained using Inturis Cardio Image 1.1 (Philips Medical Systems) software. In each case, we established the maximum diameter of the dilated artery and that of the healthy segments. Blood supply to the heart was calculated using the TIMI classification[12] and the TIMI Frame Count calculation.[13] We recorded patients´ clinical characteristics including details of age, sex, history of angina, heart attack and revascularization procedures, and cardiovascular risk factors (hypertension, diabetes, hyperlipemia, cigarette smoking), as they appeared in their case histories. Clinical and angiographic variables of patients with CE were later compared with those of patients without CE. We described significant angiographic lesions of patients in both groups. We defined these as stenosis causing a ≥70% luminal reduction in comparison to that of the normal reference segment.

Statistical analysis

Continuous variables were expressed as mean±SD, and categorical variables as absolute value and percen-
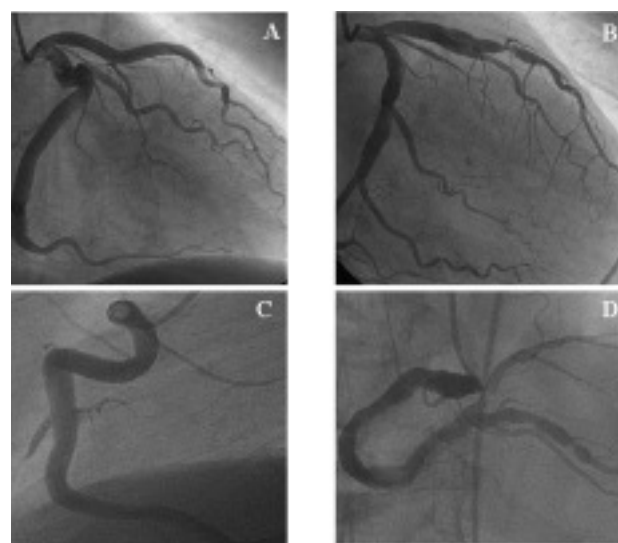

Fig. 1. Examples of coronary artery ectasia. A: Left coronary angiogram, oblique anterior right 30º projection which shows ectasia in ADA and CX, without angiographically significant stenosis. B: Left coronary angiogram, oblique anterior right 30º projection; ectasia affecting ADA and CX, with acute localized stenosis in the mid-third of ADA. C: Right coronary angiogram, oblique anterior left 90º projection showing RCA with ectasia, but without lesions. D: Posteroanterior cranial projection; RCA with ectasia and severe lesions.
ADA indicates anterior descending artery; CX, circumflex artery; RCA, right coronary artery.

Fig. 2. Analysis of patients including distribution with respect to presence or absence of coronary artery ectasia and angiographically significant stenosis.
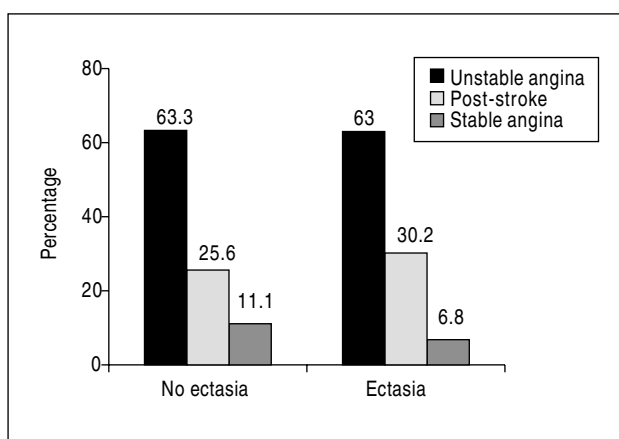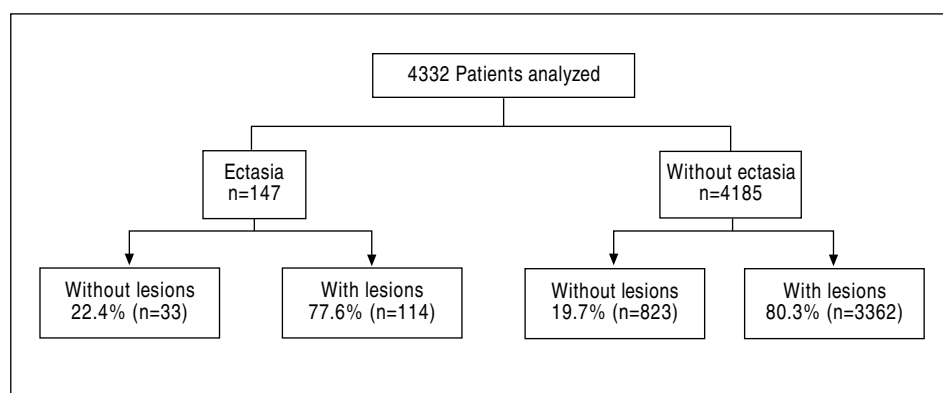

Fig. 3. Causes leading to referral for coronary angiography in patients with and without ectasia.
Stable angina: including ventricular dysfunction possibly caused by ischemia.

TABLE 1. **Clinical characteristics of patients with and without coronary artery ectasia**

	Patients with ectasia (n=147)	Patients without ectasia (n=4185)	P
Age, years	60.8±11.7	63.3±10.7	.01
Male, %	134 (91.2)	3014 (72)	<.001
HT, %	75 (51)	2235 (53.4)	NS
Hyperlipemia, %	73 (49.7)	2165 (51.7)	NS
Cigarette smoking, %	83 (56.5)	1683 (40.2)	<.001
Diabetes, %	33 (22.4)	1449 (35.1)	<.001
History of angina, %	43 (29.3)	1775 (42.4)	.01
History of infarct, %	60 (40.8)	1764 (42.2)	NS
Previous PTCA, %	12 (8.2)	754 (18)	<.001
Previous surgery, %	2 (1.4)	267 (6.4)	<.01

HT indicates hypertension; NS, nonsignificant.

tage. We compared means of independent samples using Student´s *t* test, and proportions using the chi-squared test. Statistical significance was defined as $P \leq .05$. We carried out multivariate analysis with logistical regression to analyze independent clinical predictors of the presence of CE. Data were analyzed with SPSS 10.0 software for Windows.

RESULTS

Between October 1998 and June 2001, 4709 patients underwent coronary angiographies. We included 4332 of them in the study, and 147 of these presented with CE, which represents a prevalence of 3.39% (95% CI, 2.87-3.97) (Figure 2).

Clinical characteristics

Characteristics of patients with and without CE appear in Table 1. Most of those with CE were men, smokers, with an average age markedly below that of patients without CE. They presented a lower prevalen-

ce of both diabetes and prior revascularization. Most patients were referred for coronary angiography because of unstable angina or chest pain (63% of patients with CE; 63.3% without CE) (Figure 3). In the remaining cases, angiography was carried out after myocardial infarct (30.1% and 25.6%, respectively), or to investigate stable angina or a ventricular dysfunction caused by ischemia (6.8% and 11.1%, respectively).

Angiographic characteristics

Thirty-three patients (22.4%) (95% CI, 16-30.1) presented with CE but without significant lesions to coronary arteries. In contrast, results of the angiographies indicated that most patients with CE, (77.6%) (95% CI, 69.9-84) presented significant stenosis in one (47%), two (37%) or three vessels (16%). Normally, CE affected one artery (49.7%), but two arteries were affected in 23.1% of the patients, and three were affected in 27.2%. The RCA was most frequently affected(132 patients), followed by the ADA (72 patients), and the CX

TABLE 2. **Maximum diameters of affected areas of vessels with coronary artery ectasia and of normal reference segments**

Artery	Ectasia (mm)	Normal segment (mm)	Ectasia/normal diameter ratio
Anterior descending	5.36±1.1	2.79±0.4	1.9
Circumflex	4.91±1.3	2.43±0.4	2
Right coronary artery	5.71±1.1	2.81±0.5	2

TABLE 3. **Angiographic characteristics of vessels with ectasia but without coronary artery stenosis**

Artery	Diameter ectasia/ normal vessel (mm)	Flow (TIMI/TFC)	Blood flow stasis (%)
ADA	5.20±1.1/2.61±0.4	2.6±0.4/33.1±23	54.2
CX	4.76±1.3/2.10±0.4	2.8±0.2/25.7±23	31.3
RCA	5.61±0.9/2.54±0.4	2.8±0.2/23.1±15	67.7

TFC indicates TIMI Frame Count; ADA, anterior descending artery; CX, circumflex artery; RCA, right coronary artery.

(50 patients). The RCA presented the greatest degree of dilation, and higher levels of stasis of blood flow, and of contrast retention (Tables 2 and 3).

Differences between patients with CE and without CE

Men were in the majority in both groups. However, the proportion of men was significantly greater among patients with CE (91.2% vs 72%; *P*<.001). Proportions of the cardiovascular risk factors hypertension, hyperlipemia, family antecedents and history of infarct were similar. A history of smoking was more frequent among patients with CE (56.5% vs 40.2%; *P*<.001), whereas diabetes was less common (22.4% vs 35.1%; *P*<.001). Patients with CE showed a lower prevalence of prior revascularization, whether by angioplasty (8.2% vs 18%; *P*<.001) or surgery (1.4% vs 6.4%; *P*<.01).

In our series, 22.4% of patients with CE did not present coronary artery stenosis. Nineteen percent of the patients with angiographically significant lesions presented ischemic heart disease.

Despite the absence of stenosis, some patients with CE presented functional alteration, with slowing and stasis of the blood flow (Table 3).

A logistical regression model of the variables studied (age, gender, diabetes, hypertension, hyperlipemia, cigarette smoking, family history) showed that male sex was the only variable associated with the presence of CE (hazard ratio [HR]=3.33; 95% CI, 1.81-6.13). Diabetes was the only variable independently associated with the absence of CE (HR=0.65; 95% CI, 0.43-0.98) (Table 4; Figure 4).

TABLE 4. **Clinical variables included in the logistical regression model used to determine characteristics independently associated with the existence of coronary artery ectasia (CE)**

Variables	Odds ratio	95% CI	P
Age, years	0.97	0.97-1.01	ns
Male	3.33	1.81-6.13	<.01
Diabetes	0.65	0.43-0.98	.03
Hypertension	1.16	0.83-1.64	ns
Hyperlipemia	0.94	0.67-1.32	ns
Cigarette smoking	1.28	0.89-1.84	ns
Family history	0.98	0.49-1.98	ns

NS: nonsignificant.

Follow-up of patients with CE

Patients with CE were evaluated clinically with an average follow-up of 25.6±9.3 months. The 33 patients with CE but without lesions received medical treatment. Two died (6.1%) during the follow-up period. Of the remaining 31 patients, seven continued to be completely asymptomatic (22.5%); 22 patients (71%) improved despite occasional angina; two patients (6.1%) reported symptoms identical to those recorded prior to the coronary angiography. During follow-up, two of the 31 surviving patients (6.5%) were readmitted for angina. Eight of the 114 patients with CE and associated coronary artery lesions received pharmacological treatment (7%). Nine underwent revascularization surgically (8%) and 97 by angioplasty (85%). During the long-term follow-up, eight patients died (7%), 56 of the 106 survivors were classified as asymptomatic (52%), 44 showed clear signs of improvement (41.5%), and six were considered stable (5.7%). Six survivors were readmitted for angina during the follow-up (5.7%) and angioplasty was repeated in 5 cases.

DISCUSSION

The prevalence of CE in our series (3.39%) lies in the middle of the range described in the literature. It is greater than that reported in the earliest series,[3] lower than that described in studies carried out in India,[14] and similar to that found in research in Europe and the US.[4,5]

The definition of CE implies the existence of dilation ≥1.5-fold the normal diameter of the vessel. Among the patients in our study the diameter of the artery was as much as twice that found in patients without CE. Moreover, as in the series reported by Papadakis et al,[15] coronary artery blood flow calculated with the TIMI Frame Count was slower in patients with CE. Although structural alterations (breakdown of the vessel wall, dilation of the artery) could explain
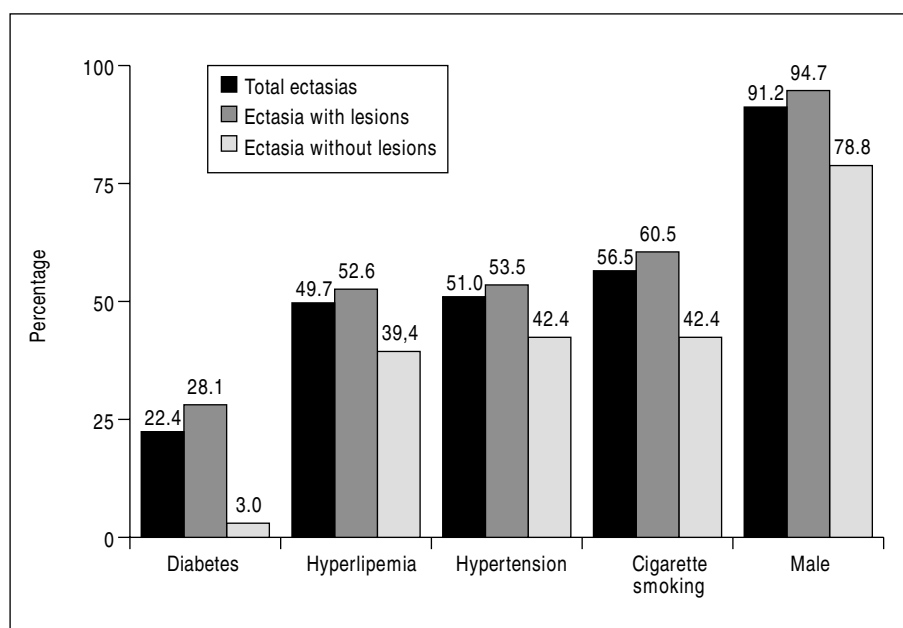
Fig. 4. Percentage of male patients and presence of cardiovascular risk factors. Analysis of all patients with ectasia and of patients with ectasia but without coronary artery lesions.

the tendency to provoke thrombosis and vasospasm, this slower blood flow may be the cause of the symptoms of angina and might even be one of the factors involved in the alterations that cause myocardial infarct in some patients with CE.[16]

Given that the mechanism that causes CE is not clearly understood, it is important we investigate the risk factors in these patients which could influence the appearance of this condition. In our series, after correction for other variables, male sex and the absence of diabetes were the only variables independently associated with CE.

Patients with CE are predominately men,[5] and in our study they represent 91.2% of all cases. Sudhir et al[17] found a higher prevalence of CE in patients with a family history of high blood cholesterol. In our study, percentages of hyperlipemia (49.7%) and hypertension (51%) were high, but similar to those of patients with ischemic heart disease and without CE, which is consistent with other findings.[5] However, there were significantly more smokers among patients with CE.

Prior revascularization was significantly lower in the group with CE, and this may have a variety of causes. We recognize that the population was relatively young, that most patients had only recently been diagnosed, that they had undergone coronary angiography for the first time, and that CE had been diagnosed through this procedure. However, in some cases medical treatment would have been chosen as they presented with nonsignificant stenosis or diffuse conditions.

Although the number of patients analyzed is as yet insufficient, the ≥2 year follow-up offers a less optimistic prognosis that could have been expected. Mortality rates were 6% among patients with CE and

without lesions, and 7% among patients with significant stenosis. These data coincide with the results of a 5-year follow-up described by Cokkinos et al,[5] these authors reported mortality rates of 10% and 9.5%, respectively, similar to the 11.9% rate among patients without CE but with acute coronary artery stenosis.

One significant finding, not previously reported, was the minimal prevalence of diabetes among patients with CE. The percentage was especially low among those with CE but without lesions (3%). It was also low among patients with CE and coronary artery stenosis (28.1%). In both cases, it was significantly lower than among patients without CE, and in these groups diabetes was present in 19% and 39%, respectively. This is not easily explained. Coronary artery ectasia seems to be a distinctive form of coronary artery atherosclerosis,[4,16] caused by the action of different risk factors based on a genetic predisposition. This would lead to initial endothelial damage activating a series of inflammatory mediators (macrophages, metalloproteins, etc) that cause degeneration of the medial layer of the vessel. These structural alterations, together with the action of nitric oxide and other vasodilators, lead to a dilation of the coronary artery: an extreme form of «positive remodeling».[19,20] However, among diabetic patients we found more cases of coronary arteries with diffuse conditions and «negative remodeling», without large amounts of plaque, but with luminal reduction and a decrease in the size of the vessel.[21] One explanation might lie in the association of diabetes with a reduction in endothelium-dependent vasodilation, caused by alterations in the synthesis and inhibition of nitric oxide,[22] which seems to play a significant role in the genesis of CE. Diabetes mellitus primarily affects the in-

timal, but not the medial layer of the vessel, thus causing «negative remodeling». It seems reasonable to hypothesize that positive remodeling appears in recently developed lesions, whereas negative remodeling occurs at a later stage, after structural changes. Perhaps diabetic patients tend to develop a more aggressive, evolved form of atherosclerosis,[23,24] whereas alterations in lipoprotein metabolism are more closely associated with the phenomenon of positive remodeling.[25] We can probably add to these risk factors the existence of a certain genetic predisposition, as men make up more than 90% of the patients with CE. Studies that enable us to clarify this genetic factor and explain the exact mechanisms that cause CE are needed.

Limitations

Although the number of patients with CE in our study makes this one of the largest series reported, it is not enough, and this may limit the statistical value of the tests used to detect variables associated with the presence of CE.

It is difficult to estimate the prevalence of this condition in the population at large. The descriptive nature of our research, based on a series of patients referred to the hemodynamics laboratory for different reasons does not enable us to establish the real prevalence of CE given that it probably exists in forms that are barely symptomatic or even asymptomatic, and which therefore are not studied angiographically. We excluded patients with valvular complaints or cardiomyopathies, as well as borderline cases, which may have led us to underestimate the number of patients with CE.

CONCLUSIONS

In our setting, 3.39% of the patients who undergo coronary angiography to test for ischemic heart disease present with CE and most of these are men. Coronary artery ectasia is associated with the traditional risk factors, except diabetes. This appears less frequently than normal among patients with associated coronary artery lesions, and infrequently in patients presenting an isolated form of CE without stenosis.

Further studies are needed to determine the most appropriate therapy and long-term prognosis.

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