Scientific letters

Acute Myocardial Infarction in Patients With a Very Rare Form of Anomalous Origin of the Left Main Coronary Artery

Infarto agudo de miocardio en pacientes con forma muy rara de origen anómalo de la arteria coronaria principal izquierda

To the Editor,

We present the case of a 50-year-old man (case 1) with hypertension and smoking habits, who presented with an ongoing chest pain for 2 h and an ST-segment elevation on the antero-septal and lateral leads on the electrocardiogram, who underwent urgent cardiac catheterization.

The coronary angiography revealed a dominant right coronary artery with no stenosis (Fig. 1A). The left main coronary artery (LMCA) was found to originate from the right coronary sinus, with a separate ostium from the right coronary artery and a retroaortic course. Severe lesions in the middle and distal-shafts of the LMCA were disclosed (Fig. 1B, white arrow). The anomalous LMCA was easily cannulated with a Judkins Left 4.0 catheter and successfully stented (Fig. 1C).

Acute pulmonary edema in the context of a hypertensive crisis, requiring mechanical ventilation, occurred in the immediate period after revascularization. Maximum troponin I levels were found to be 185.9 μg/L. Recovery was uneventful and the left ventricular systolic function was only mildly compromised at discharge. Multislice computed tomography coronary angiography confirmed an LMCA retroaortic course (Figs. 1D and E, black arrows) and coronary stent patency (Fig. 1F, arrowhead).

We also report the case of a 68-year-old man with hypertension, presented to the emergency department with ongoing chest pain. The electrocardiogram showed a left ventricular strain pattern with a left anterior fascicular hemiblock; the cardiac troponin I levels were found to be elevated (3.6 μg/L) and the patient was admitted for a non-ST elevation acute myocardial infarction. The chest pain was refractory to maximum anti-ischemic therapy and urgent coronary angiography was performed. During cardiac catheterization, the patient's condition progressed to cardiogenic shock, requiring inotropic support and mechanical ventilation. The right coronary artery was a dominant vessel with a mild distal lesion (Fig. 2A), but the LMCA was arising from the right coronary sinus with a retroaortic course (Fig. 2B, white arrow). The LMCA had a middle-shaft severe stenosis (Fig. 2C, white arrow), and the left anterior descending artery had a proximal critical lesion and was occluded at the middle segment (Fig. 2C, black arrow). LMCA cannulation was attempted without success with guiding catheters XB 3.5, Judkins Left 4.0, and Judkins Left 5.0. Finally, a multipurpose A1 catheter, allowed successful stent angioplasty of the anomalous LMCA and the left anterior descending artery (Fig. 2D, white and black arrows). Hemodynamic improvement was immediate, allowing removal of inotropic support and mechanical ventilation within 24 h. Recovery was uneventful and the patient was discharged with recovered left ventricle function. The patient did not cooperate to perform multislice computed tomography coronary angiography.

Most of the coronary anomalies are found incidentally in 0.6% to 1.3% coronary angiographies. Origin of the LMCA from the right
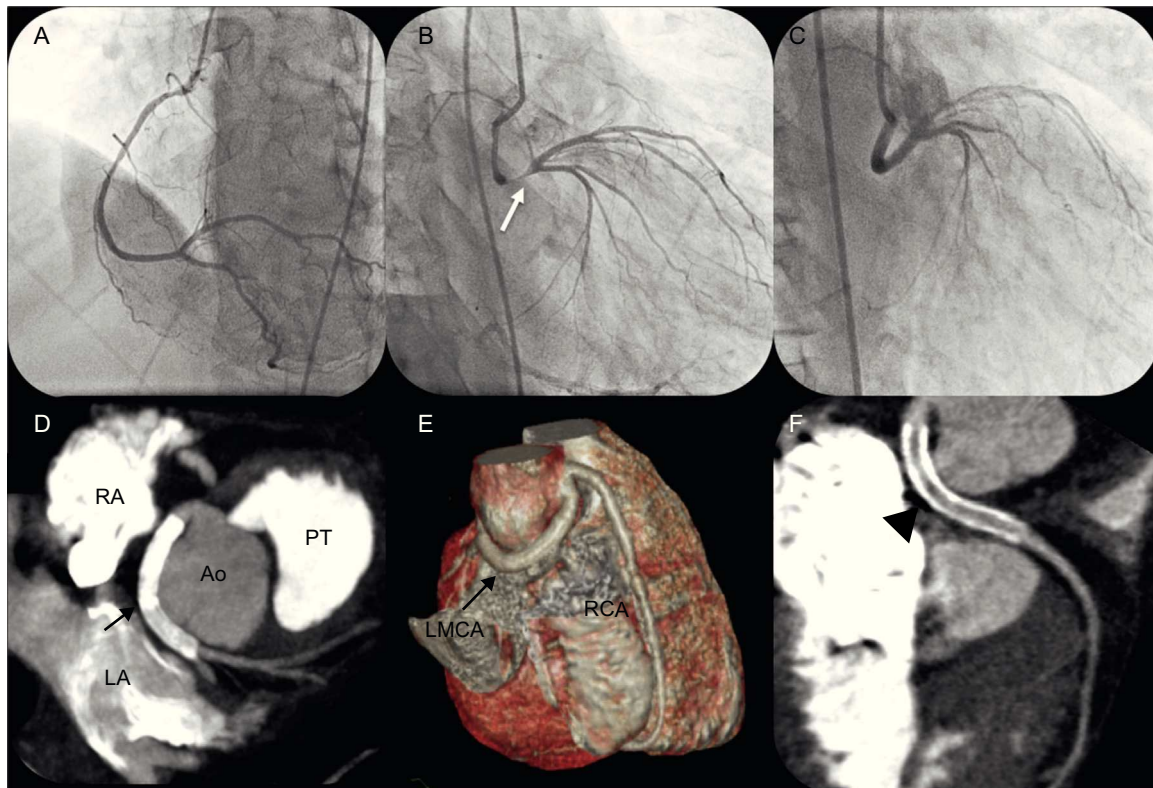

Figure 1. A-C: Coronary angiography. D-F: Multislice computed tomography coronary angiography. Ao, aorta; LA, left atrium; LMCA, left main coronary artery; PT, pulmonary trunk; RA, right atrium; RCA, right coronary artery.
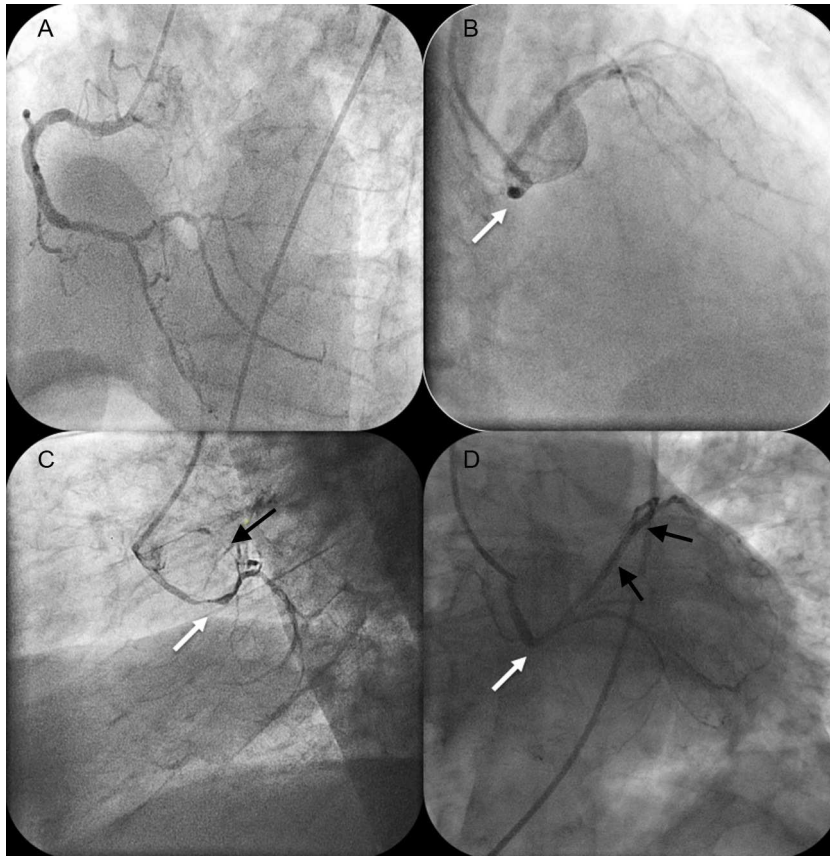
Figure 2. Coronary angiography.

coronary sinus is an extremely rare anomaly with an incidence of 0.017%.[1]

It is fundamental to identify the course of the anomalous LMCA: retroaortic, interarterial, septal, or anterior to the right ventricle free wall.[1] Major prognostic relevance is attributed to the interarterial course of the LMCA, which is associated with sudden cardiac death, particularly during or immediately after strenuous physical exercise, as a result of coronary compression.[2]

The retroaortic course of the LMCA is a less frequent trajectory and is usually found to be benign,[1] although it can seldom present with angina or even acute myocardial infarction.[3] A multifactorial approach has been proposed to explain ischemia associated to the anomalous origin of the LMCA: slit-like coronary orifice with dynamic obstruction, acute angle take-off, or intramural segments of the anomalous coronary artery.[3] However, in our cases, severe atherosclerotic coronary disease was disclosed, raising the hypothesis of an early atherosclerotic degeneration process, as seen in other coronaries with anomalous origin in the right coronary sinus, like the circumflex artery.[4] In the RACES registry (a registry of 13 Spanish hospitals), atherosclerotic coronary disease (in any coronary) was found in association with 51% of patients[5], although the true relationship between atherosclerotic coronary disease and coronary anomalies is unknown. In case 1, no additional atherosclerotic coronary disease was found and so, theoretically, an LMCA spasm could have been present.

Primary coronary angioplasty of an anomalous coronary artery is a challenging and highly complex intervention, particularly in the emergency setting. For a successful primary coronary angioplasty, it is fundamental to immediately and accurately recognize the anatomical details of the anomalous vessel.[3]

The retroaortic course of the LMCA, on coronary angiography, is identified by the visualization of the "dot sign"; it represents the artery visible at the end, posterior to the aortic root, on a 30° right anterior oblique incidence.[6] However, the anomalous LMCA relation to the great vessels may be difficult to recognize because of the lack of a 3-dimensional visualization, only possible through multislice computed tomography coronary angiography.

This imaging technique can provide a more complete assessment of the origin, course, and anatomical relationship of the anomalous coronary with its neighboring structures, which is considerably relevant in the diagnosis and delineation of coronary intervention.[2,3] It has the disadvantage of not being possible to perform in acute settings, as these require an emergency intervention.

A suitable selection of guide catheters, allowing a good coaxial alignment and backup support, is also essential for successful outcomes in anomalous LMCA angioplasty.[3] Other types of guide catheters have been described previously[3] and are selected on a case-by-case basis.

Cláudia Jorge,* José António Duarte, Pedro Cardoso, Ana G. Almeida, Pedro Canas da Silva, and António Nunes Diogo

Serviço de Cardiologia, Hospital Universitário de Santa Maria, Lisbon, Portugal

* Corresponding author:
E-mail address: c_jorge@sapo.pt (C. Jorge).

REFERENCES

1. Yamanaka O, Hobbs RE. Coronary artery anomalies in 126,595 patients undergoing coronary arteriography. Cath Cardiovasc Diagn. 1990;21:28–40.

2. Balaguer-Malfagón JR, Estornell-Erill J, Vilar-Herrero J, Pomar-Domingo F, Frederico-Zaragoza P, Payá-Serrano R. Arteria coronaria izquierda anómala en el seno de Valsalva derecho asociada a ateromatosis coronaria. Rev Esp Cardiol. 2005;58:1351–4.

3. Vijayvergiya R, Grover A, Singhal M. Percutaneous revascularization in a patient with anomalous origin of the left main coronary artery. World J Cardiol. 2011; 3:311–4.

4. Donaldson RM, Raphael M, Radley-Smith R, Yacoub MH, Ross DN. Angiographic identification of primary coronary anomalies causing impaired myocardial infarction. Cathet Cardiovasc Diagn. 1983;9:237–49.

5. Barriales-Villa R, Morís C, Sanmartín JC, Fernández E, Palín F, Ruiz Nodar JM. Registro de anomalías congénitas de las arterias coronarias con origen en el seno de Valsalva contralateral en 13 hospitales españoles (RACES). Rev Esp Cardiol. 2006;59:620–3.

6. Serota H, Brath CW, 3rd, Seuc CA, Vandormael M, Aguirre F, Kern MJ. Rapid identification of the course of anomalous coronary arteries in adults: the "dot and eye" method. Am J Cardiol. 1990;65:891–8.

Usefulness of Genetic Testing for Hypertrophic Cardiomyopathy in Real-world Practice

Utilidad del análisis genético de la miocardiopatía hipertrófica en la práctica real

To the Editor,

Hypertrophic cardiomyopathy (HCM) is a genetic disease caused by mutations in at least 11 genes that primarily code for cardiac sarcomere proteins.[1] Historically, the management of this disease has involved systematic evaluation of the individual's first-degree relatives over many years. Since the first report of a mutation associated with HCM in 1990, genetic analysis has progressed from research to clinical practice. Currently, knowledge of the causative mutation in an individual with HCM does not usually imply changes to the therapeutic approach. However, detection of the genetic defect can have important implications, because patients and their families can be offered effective genetic counselling.[2] Furthermore, early identification of the mutation in relatives allows closer monitoring and early detection of complications. Finally, relatives without the mutation can be excluded, thereby avoiding unnecessary follow-up.[1,2] The systematic use of genetic testing for HMC has been shown to be cost-effective in theoretical models applied in Anglo-Saxon countries,[3] but no data are available from Spain.

The aim of the present study was to evaluate the clinical and economic impact of genetic analysis of the relatives of HCM patients in Spain. To do this, we performed an observational study of families with HCM who underwent genetic testing from 2008 to 2011 in 2 inherited cardiovascular disease units.

We evaluated the clinical utility of genetic testing (reproductive, professional, and sports counselling) and the direct economic savings derived from the cessation of follow-up of relatives with a negative test result. During the study period, genetic testing was performed in 171 index patients with HCM (118 [68%] men; mean age, 52 [17] years). In all patients, the exons and intronic flanking regions of the 5 genes most frequently involved in HCM (*MYH7, MYBPC3, TPM1, TNNI3,* and *TNNT2*) were analyzed using Sanger sequencing. A further 4 genes (*ACTC, MYL2, MYL3,* and *TNNC1*) were analyzed in 43 index patients (25%), and 2 further genes (*PRKAG2* and *LAMP2*) were analyzed in 4 patients. The causative mutation was identified in 82 index patients (48%). Patients who had variants of uncertain significance were excluded from the study.

A clinical evaluation (with electrocardiograms and echocardiograms) plus cascade genetic screening was then undertaken in relatives who wished to be included in the study. In total, 228 family members were evaluated (2.8 relatives/index patient; mean age, 39 [19] years). Of these, 106 relatives (46.5%) were carriers of the same mutation as the index patient (positive genotype). In contrast, 122 relatives (53.5%) did not have the mutation (negative genotype) and, after receiving genetic counselling, were given definitive clearance (Figure).

Genetic counselling includes reproductive, professional, and sports advice. The assessment team should include experienced professionals. The risks and benefits of testing, as well as its clinical, psychological, and social implications, should be clearly explained to patients and their relatives. Reproductive counselling should ideally be completed before pregnancy. Counselling should address issues such as the inheritance pattern, penetrance, expressivity, and familial history. All participants found to be carriers of a causative mutation must be informed of alternative reproductive methods.

To evaluate the study participants who would benefit from reproductive advice, the cut-off for reproductive age was set at 40 years. Thus, 42% of the participants with mutations (78 patients) were younger than 40 years and therefore received reproductive counselling. Relatives who were noncarriers also benefited from reproductive counselling. In the present study, almost half (48%) of the relatives with a negative genotype (59 relatives) were younger than 40 years and were therefore informed that their descendants would not have the disease (Figure).

The European Society of Cardiology advises against participation in competitive sports activity in persons with a positive genotype and negative phenotype,[4] but provides no recommendations on professional activities. However, given the high probability that genetic carriers will develop the phenotype at some point in their lives, it seems reasonable to advise against professions that HCM patients would be unable to carry out (police, fire-fighter, pilot, etc.), as well as against participation in competitive sports involving intense physical activity.

In the study population, 25 relatives with a positive genotype and a negative phenotype (24%) and 30 relatives with a negative genotype (25%) were younger than 30 years old and were therefore advised about their profession and sporting practices (Figure).

Finally, we determined the economic costs of genetic testing, such as the difference between the cost of genetic tests vs the savings in consultations, electrocardiograms, and echocardiograms among genotype-negative relatives who discontinue the periodic monitoring recommended by clinical practice guidelines.[1,2] The costs of the genetic analysis and other tests were calculated from the mean rate charged by 2 companies and by the official costs in Spanish autonomous communities (Table).[5,6]

After detailed clinical investigation to identify families who could potentially have multiple mutations, 122 relatives with the negative genotype were given definitive clearance.

The total expenditure on genetic screening was €323 988. As shown in the Table, the savings derived from the cessation of monitoring of genotype-negative relatives amounted to €300 913 (€3167 [1906] per relative participating in the study).[5,6] The estimated direct cost of genetic analysis (cost of genetic analysis minus direct health care savings) was €23 075. The cost of each relative undergoing genetic analysis was therefore €135.

The present study demonstrates both the clinical and economic viability of genetic testing for HCM in Spain. This study did not consider the potential savings in other types of test (cardiac