

these authors, which showed features consistent with arrhythmogenic cardiomyopathy (carriers of a *DSP* mutation), there was no second mutational event in our patient that could be related to the risk of sudden death and make this association more plausible.

Detection of noncompaction in patients with ASD could alert to the possible presence of this entity, which has a malignant character.

Julían Palomino Doza,* Rafael Salguero-Bodes, María de la Parte, and Fernando Arribas-Ynsaurriaga

Unidad de Cardiopatías Familiares, Hospital Universitario 12 de Octubre, Madrid, Spain

*Corresponding author:

E-mail address: julian.palomino@salud.madrid.org (J. Palomino Doza).

Available online 17 March 2017

REFERENCES

- Bermúdez-Jiménez FJ, Jiménez-Jáimez J, López-Fernández S. Overlap of arrhythmogenic cardiomyopathy, spongiform cardiomyopathy, and congenital heart disease. *Rev Esp Cardiol.* 2017;70:51.
- Ueyama T, Kasahara H, Ishiwata T, et al. Myocardin expression is regulated by Nkx2.5, and its function is required for cardiomyogenesis. *Mol Cell Biol.* 2003;23:9222–9232.
- Kasahara H, Benson DW. Biochemical analyses of eight NKX2.5 homeodomain missense mutations causing atrioventricular block and cardiac anomalies. *Cardiovasc Res.* 2004;64:40–51.
- Ouyang P, Saarel E, Bai Y, et al. A de novo mutation in NKX2.5 associated with atrial septal defects, ventricular noncompaction, syncope and sudden death. *Clin Chim Acta.* 2011;412:170–175.
- Maury P, Gandjbakhch E, Baruteau A, et al. Cardiac phenotype and prognosis of patients with mutations in NKX2.5 gene [abstract]. *Eur Heart J.* 2016;37(Suppl 1):207.

<http://dx.doi.org/10.1016/j.rec.2017.02.032>

1885-5857/

© 2016 Sociedad Española de Cardiología. Published by Elsevier España, S.L.U. All rights reserved.

Diagnostic and Prognostic Findings in Patients With Positive Clinical or ECG Exercise Tests in the Absence of Echocardiographic Abnormalities



Hallazgos diagnósticos y pronósticos en pacientes con prueba de esfuerzo clínica o ECG positivos pero ecocardiografía negativa

To the Editor,

Although normal findings on exercise echocardiography (EE) are considered indicative of a good prognosis,^{1,2} there is little information on the prognosis of patients who have a normal EE together with positive clinical or electrocardiography (ECG) findings. Our aim was to evaluate the prognosis and angiographic results of patients in the following situations: EE (–) in the absence of positive clinical or ECG findings (negative group), EE (–) with

Table

Clinical Characteristics and Exercise Echocardiography Results in 7127 Patients

	All (n = 7127)	Clinical and ECG (–) (n = 6133)	Clinical or ECG (+) (n = 892)	Clinical and ECG (+) (n = 102)	P
<i>Clinical characteristics</i>					
Age, years	61 ± 13	60 ± 13	63 ± 11	63 ± 10	< .001
Women	3393 (48)	2927 (48)	425 (48)	41 (40)	NS
Diabetes mellitus	1141 (16)	949 (15)	163 (18)	29 (28)	< .001
Hypertension	3769 (53)	3200 (52)	507 (57)	62 (61)	.009
Smoking	1559 (22)	1379 (22)	159 (18)	21 (21)	.007
Hypercholesterolemia	3380 (47)	2870 (47)	448 (50)	62 (61)	.004
Atrial fibrillation	326 (5)	282 (5)	38 (4)	6 (6)	NS
ECG nonassessable	1276 (18)	1173 (19)	103 (12)	—	—
History of CAD	971 (14)	796 (13)	143 (16)	32 (31)	< .001
Typical angina	391 (5)	274 (4)	93 (10)	24 (24)	< .001
<i>Medications</i>					
ACEIs/ARBs	2159 (30)	1825 (30)	293 (33)	41 (40)	.02
Nitrites	1307 (18)	1054 (17)	208 (23)	45 (44)	< .001
Calcium channel blockers	632 (9)	520 (8)	95 (11)	17 (17)	.002
Beta blockers*	540 (8)	437 (7)	84 (9)	19 (19)	< .001
Baseline LVEF, %	61 ± 4	61 ± 5	61 ± 4	61 ± 3	NS
<i>Exercise echocardiography</i>					
MET	9.8 ± 3.3	9.8 ± 3.3	9.3 ± 3.1	9.1 ± 2.7	< .001
Submaximal test	1243 (17)	1020 (17)	194 (22)	29 (28)	< .001
Double peak product × 10 ³	25.5 ± 5.9	25.6 ± 5.9	25.1 ± 6.0	24.3 ± 5.5	.004
LVEF peak, %	69 ± 6	69 ± 6	68 ± 5	69 ± 3	< .001
LVEF increase, %	8 ± 3	8 ± 3	8 ± 3	8 ± 2	< .001

ACEIs, angiotensin converting enzyme inhibitors; ARBs angiotensin II receptor blockers; CAD, coronary arterial disease; ECG, electrocardiogram; LVEF, left ventricular ejection fraction; MET, metabolic equivalents; NS, not significant.

The values express n (%) or mean ± standard deviation.

* At the time of exercise echocardiography.

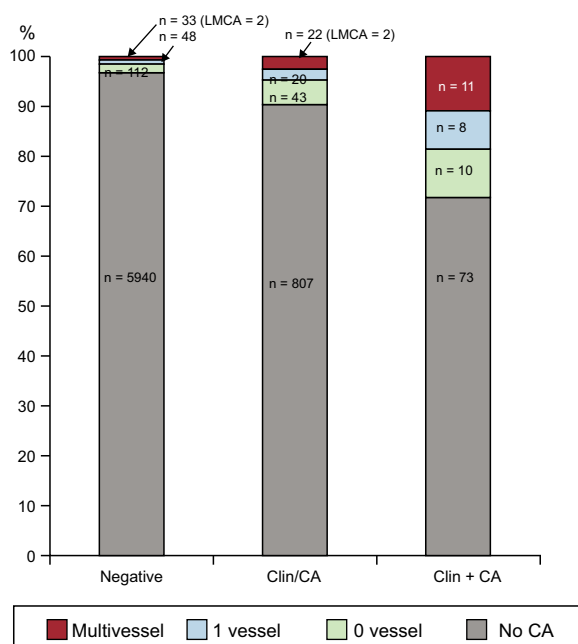


Figure. Percentage of patients with a normal coronary angiogram, with coronary artery disease, and not referred for coronary angiography in the 3 groups. CA, coronary angiography; LMCA, left main coronary artery. gr1.

positive clinical or ECG results (Clin/ECG group), and EE (–) with positive clinical and ECG findings (Clin+ECG group).

A retrospective analysis was performed of patients with normal EE results. Of 17 225 patients undergoing treadmill EE, those with positive findings, cardiomyopathy, moderate or severe valvular disease, or age younger than 18 years were excluded. The final population included 7127 patients with a normal first EE, defined as the absence of regional contraction abnormalities at rest and on exercise.^{3,4} Positive clinical findings were defined as precordial pain consistent with angina, or significant and limiting dyspnea during exercise. In patients with an assessable ECG, the test was considered positive when a horizontal or downsloping ST segment depression of ≥ 1 mm after the J point was observed in at least 1 lead, or an upsloping was seen in patients with no previous infarction.⁴ The ECG was considered nonassessable in patients with baseline ST abnormalities, left bundle branch block, digoxin treatment, or Wolff-Parkinson-White syndrome. We evaluated major cardiac events before revascularization, defined as cardiac death or nonfatal acute myocardial infarction, as well as revascularizations during follow-up. Furthermore, we evaluated the coronary angiograms performed in the 6 months following EE testing. Coronary artery disease (CAD) was defined as $\geq 50\%$ luminal narrowing of a main coronary artery, a major branch, or a coronary arterial or venous graft, determined visually.

The clinical characteristics and EE results of the 3 groups of patients are shown in Table. There were 102 patients in the Clin+ECG group (1.4%), 892 in Clin/ECG (12.5%), and 6133 in the negative group (86.1%). Over a median follow-up of 2.1 [interquartile range, 0–6.7] years, there were 419 major cardiac events, with no differences between the groups (annualized major cardiac event rates, 1.2%, 1.4%, and 1.1% in groups Clin+ECG, Clin/ECG, and negative, respectively). However, the annualized revascularization rates were higher in the positive groups (9.2% Clin+ECG, 2.9% Clin/ECG, and 1.4% negative group; $P < .001$). Following EE testing, coronary angiography (total, 4.3%) was carried out more frequently

in the positive groups (28% Clin+ECG, 9.5% Clin/ECG, and 3.1% negative group; $P < .001$), and the positive groups had higher percentages of angiograms showing CAD (66% Clin+ECG, 49% Clin/ECG, and 42% negative group; $P < .001$). Nonetheless, the rates of left main CAD and multivessel disease were very low (Figure).

The results of this study support the notion that a negative EE has excellent prognostic value.^{1,2} Of note, when each component evaluated was normal (absence of clinical findings, and negative ECG and EE), even the revascularization requirement was minimal. Some patients with positive clinical and ECG findings had CAD, but it was usually single-vessel disease and the affected territories that were not dependent on the left anterior descending artery. This is because EE is very sensitive for detecting multivessel disease and left anterior descending artery disease but is not as sensitive for single-vessel disease or disease affecting the right coronary or circumflex arteries. In a recent study performed in EE (–) patients, a positive ECG was not associated with a larger number of events or revascularizations,⁵ although the results might have been different if patients had been positive both clinically and on ECG. Thus, although events do not seem to be associated with positive status other than image-related, this group may benefit from coronary revascularization. For patients who are less likely to benefit from coronary angiography and eventual revascularization, such as those showing only clinical or only ECG findings, coronary computed tomography examination could be considered,⁶ since “blank” coronary angiograms were not uncommon in this subgroup.

Jesús Peteiro,^{a,*} Alberto Bouzas-Mosquera,^a Javier Broullón,^b Dolores Martínez,^a and José M. Vázquez-Rodríguez^a

^aServicio de Cardiología, Complejo Hospitalario Universitario de A Coruña (CHUAC), Instituto de Investigación Biomédica de A Coruña (INIBIC) y Universidad de A Coruña, A Coruña, Spain

^bServicio de Informática, Complejo Hospitalario Universitario de A Coruña (CHUAC), Instituto de Investigación Biomédica de A Coruña (INIBIC) y Universidad de A Coruña, A Coruña, Spain

*Corresponding author:

E-mail address: pete@canalejo.org (J. Peteiro).

Available online 14 April 2017

REFERENCES

- Metz LD, Beattie M, Hom R, Redberg RF, Grady D, Fleischmann KE. The prognostic value of normal exercise myocardial perfusion imaging and exercise echocardiography: a meta-analysis. *J Am Coll Cardiol.* 2007;49:227–237.
- McCully RB, Roger VL, Mahoney DW, et al. Outcome after normal exercise echocardiography and predictors of subsequent cardiac events: follow-up of 1,325 patients. *J Am Coll Cardiol.* 1998;31:144–149.
- Peteiro-Vázquez J, Monserrat-Iglesias L, Mariñas-Davila J, et al. Valor pronóstico de la ecocardiografía de ejercicio en cinta rodante. *Rev Esp Cardiol.* 2005;58:924–933.
- Peteiro J, Bouzas-Mosquera A, Broullón FJ, García-Campos A, Pazos P, Castro-Beiras A. Prognostic value of peak and post-exercise treadmill exercise echocardiography in patients with known or suspected coronary artery disease. *Eur Heart J.* 2010;31:187–195.
- Kobal SL, Wilkoff-Segev R, Patchett MS, et al. Prognostic value of myocardial ischemic electrocardiographic response in patients with normal stress echocardiographic study. *Am J Cardiol.* 2014;113:945–949.
- Marcus R, Ruff C, Burgstahler C, et al. Evidencia científica reciente y avances técnicos en la tomografía computarizada cardiovascular. *Rev Esp Cardiol.* 2016;69:509–514.

<http://dx.doi.org/10.1016/j.rec.2017.03.021>

1885-5857/

© 2016 Sociedad Española de Cardiología. Published by Elsevier España, S.L.U. All rights reserved.