Table 2
Prevalence of Atrial Fibrillation by Age Groups and Sex

Age group	Individuals, n	Prevalence of atrial fibrillation, % (n)		
		Males	Females	Total
16-29 y	2263	0	0	0
Males	1612			
Females	651			
30-39 y	4403	0.062 (2)	0	0.045 (2)
Males	3221			
Females	1182			
40-49 y	3900	0.071 (2)	0	0.051 (2)
Males	2807			
Females	1093			
50-59 y	2095	0.187 (3)	0.203 (1)	0.191 (4)
Males	1602			
Females	493			
60-74 y	518	0.688 (3)	0	0.579 (3)
Males	436			
Females	82			
16-74 y	13,179	0.103 (10)	0.029 (1)	0.083 (11)
Males	9678			
Females	3501			

points to a low rate of AF in the young Spanish population, as no cases were detected on electrocardiography performed in 1220 federated athletes aged 15 to 29 years.

The interpretation of the results in this study has several limitations. Because of the methods used, it is likely that cases of transient AF were not detected. It should be noted that paroxysmal AF is particularly more common in the young population than persistent or permanent AF. This, together with the working nature of the sample, which excludes individuals with disabling heart disease, precludes extrapolation of the rates observed to the overall Spanish population and may be the reason why our rates are lower than those reported in the OFRECE[1] study in comparable age ranges. Furthermore, individuals from only 5 Spanish regions were included; hence, the data obtained do not represent the entire working population of Spain. The paucity or absence of cases in the age groups younger than 40 years indicates that the sample size does not suffice to provide a precise estimate of the prevalence of AF in the entire Spanish working population in these ages.

In conclusion, the present report analyzes the prevalence of AF in a Spanish working population cohort with a large representation of adults younger than 40 years, which contrasts with most previous studies performed in our country. Nonetheless, the small number of cases detected in those aged 40 years and younger indicates that a larger sample would be needed to achieve precise estimation of the AF prevalence in the younger Spanish working population, and this would likely be true for other samples of apparently healthy young individuals.

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REFERENCES

1. Gómez-Doblas JJ, Muñiz J, Martin JJ, et al. Prevalencia de fibrilación auricular en España. Resultados del estudio OFRECE. *Rev Esp Cardiol.* 2014;67:259–269.
2. Cea-Calvo L, Redón J, Lozano JV, et al. Prevalencia de fibrilación auricular en la población española de 60 o más años de edad. Estudio PREV-ICTUS. *Rev Esp Cardiol.* 2007;60:616–624.
3. Rodríguez-Capitán J, Fernández-Meseguer A, García-Pinilla JM, et al. Frequency of different electrocardiographic abnormalities in a large cohort of Spanish workers. *Europace.* 2016. http://dx.doi.org/10.1093/*europace*/euw283.
4. Masiá R, Sala J, Marrugat J, Pena A. Prevalencia de fibrilación auricular en la provincia de Girona: el Estudio REGICOR. *Rev Esp Cardiol.* 2001;54:1240.
5. Baena-Díez JM, Grau M, Forés R, et al. Prevalencia de fibrilación auricular y factores asociados en España, análisis de seis estudios de base poblacional. Estudio DARIOS. *Rev Clin Esp.* 2014;214:505–512.
6. Carro-Hevia A, Fernández MM, Palacio JM, Martín EH, Castro MG, Rodríguez-Reguero JJ. ECG as a part of the preparticipation screening programme: an old and still present international dilemma. *Br J Sports Med.* 2011;45:776–779.

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Causes and Predictors of Death in Atrial Fibrillation Patients Initiating Treatment With Direct Oral Anticoagulants

Causas y predictores de muerte de los pacientes con fibrilación auricular que inician tratamiento con anticoagulantes orales directos

To the Editor,

Patients with atrial fibrillation often have numerous concurrent diseases that are associated with a worse prognosis. Although several studies have addressed the causes of death in these patients, only limited data are available from clinical practice for patients under treatment with direct-acting oral anticoagulants (DAOAs). Given that patients who receive these agents in Spain usually have a different clinical profile to those who receive vitamin K antagonists,[2,3] we evaluated the causes and predictors of death in patients with nonvalvular atrial fibrillation (NVAF) who started treatment with DAOAs in 3 Spanish health areas. For our study, we included 973 consecutive patients with NVAF who were prescribed DAOA for the first time between January 2013 and December 2014. Patients were selected from the prescription database, which includes information from all medical prescriptions of all the health areas included in the study, given that

electronic prescription is mandatory. Subsequently, all electronic medical records were reviewed to check whether NVAF was present. We excluded patients with an indication for temporary anticoagulation and indications other than atrial fibrillation; patients with hypertrophic cardiomyopathy, moderate/severe rheumatic mitral stenosis, or mechanical valve prosthesis; and those who had already taken DAOAs. Patients were followed up from the date of prescription through to a common end date. The primary outcome measure was death. Information on this outcome was available for 99.8% of the patients. Deaths were reported by the clinical cardiologist, using a standard form that included a structured description of the date and place of death, circumstances in which death occurred, treatments administered, etc. The information was obtained through electronic chart review, death certificates, reports of out-of-hospital emergency personnel, and telephone contact with the family in the event of death. To identify the factors associated with death, a multivariate Cox regression analysis was undertaken, which was used to calculate the hazard ratio. SPSS v21 and STATA v13 statistical packages were used for the statistical analysis. The present study was approved by the ethics committees of the participating centers.

The characteristics of the study population are summarized in Table 1. For a mean follow-up of 646 days (range, 470-839 days), 102 deaths were recorded (5.85/100 patient-years), of which 34 were of cardiac cause (1.95/100 patient-years), 55 of noncardiac cause (3.16/100 patient-years), and 13 of undetermined cause (0.74/100 patient-years). Table 1 of the supplementary material shows the incidence of the causes of death in the study population. The most frequent causes of death were neoplasms (1.20/100 patient-years), infections (0.92/100 patient-years), and heart failure (0.80 patient-years). Patients who died were older and had more concurrent diseases and higher scores on the risk scales for thromboembolic and bleeding events (Table 1). The predictors of overall mortality, whether of cardiovascular origin or not, are shown in Table 2. The C-statistic of the model was 0.82 for overall mortality (95% confidence interval [CI], 0.77-0.87; $P < .001$), 0.81 for cardiovascular mortality (95% CI, 0.73-0.89; $P < .001$), and 0.81 for noncardiovascular mortality (95% CI, 0.74-0.87; $P < .001$) (Hosmer-Lemeshow test, $P > .05$ in the 3 models). During follow-up, mortality was similar regardless of the type of anticoagulant or cause of death (Tables 2 and 3 of the supplementary material).

This study is the first to assess the causes of death in a recent and multicenter cohort of patients with NVAF who started treatment with DAOA. Our study shows high mortality in this type of patient, and the most frequent causes of death were neoplasms, infections, and heart failure, whereas deaths due to embolic and/or bleeding events were infrequent. In contrast, the main cause of death in pivotal clinical trials was of cardiovascular origin,[1–3] which may reflect differences between the clinical profile of the patients included in clinical trials and those who receive DAOAs in daily clinical practice. We therefore believe it is useful to study the causes of death and identify specific predictors

Table 1
Baseline Characteristics of the Study Population by Survival

	Total (n = 973)	Death		*P*
		No (n = 869)	Yes (n = 102)	
Sociodemographic				
Age, y	76 ± 9	75 ± 9	81 ± 7	< .001
Caucasian race	970 (99.7)	866 (99.7)	102 (100)	.552
Female sex	529 (54.4)	471 (54.2)	57 (55.9)	.747
First episode of AF	296 (30.5)	267 (30.8)	28 (27.7)	.521
Persistent-permanent AF	602 (61.9)	527 (60.9)	73 (73.0)	.018
Cardiovascular risk factors				
Hypertension	825 (84.8)	732 (84.2)	91 (89.2)	.185
Diabetes mellitus	291 (29.9)	241 (27.7)	49 (48.0)	< .001
Current smoker	64 (6.6)	61 (7.0)	3 (2.9)	.290
Concurrent diseases				
Alcohol abuse	17 (1.7)	15 (1.7)	2 (2.0)	.864
COPD and/or asthma	182 (18.7)	153 (17.6)	29 (28.4)	.008
Stroke and/or prior TIA	197 (20.2)	164 (18.9)	33 (32.4)	.001
Systemic embolism	9 (0.9)	7 (0.8)	2 (2.0)	.249
Ischemic heart disease	118 (12.1)	97 (11.2)	21 (20.6)	.006
Prior stenting	68 (7.0)	59 (6.8)	9 (8.8)	.446
Peripheral artery disease	37 (3.8)	28 (3.2)	9 (8.8)	.005
Vascular disease	139 (14.3)	114 (13.1)	25 (24.5)	.002
Heart failure	164 (16.9)	121 (13.9)	43 (42.2)	< .001
Liver disease	7 (0.7)	6 (0.7)	1 (1.0)	.743
Chronic kidney disease[a]	339 (34.9)	289 (33.3)	50 (49.0)	.002
Renal transplant/hemodialysis	4 (0.4)	1 (0.1)	3 (2.9)	< .001
History of neoplasms	110 (11.3)	82 (9.4)	28 (27.5)	< .001
Intracranial bleeding	27 (2.8)	22 (2.5)	5 (4.9)	.168
Mayor bleeding	82 (8.4)	66 (7.6)	16 (15.7)	.005
Major digestive tract bleeding	35 (3.6)	27 (3.1)	8 (7.8)	.015
History of labile INR	243 (65.0)[b]	211 (65.7)	32 (61.5)	.556
Risk scales				
$CHADS_2$	2.3 ± 1.3	2.2 ± 1.2	3.2 ± 1.3	< .001

Table 1 *(Continued)*
Baseline Characteristics of the Study Population by Survival

	Total (n = 973)	Death		*P*
		No (n = 869)	Yes (n = 102)	
CHA_2DS_2VASc	3.9 ± 1.6	3.8 ± 1.5	5.1 ± 1.6	< .001
HAS-BLED	1.6 ± 0.9	1.6 ± 0.9	2.2 ± 0.9	< .001
Laboratory analysis and echocardiogram				
GFR (mL/min/1.73 m^2)	69 ± 20	70 ± 19	62 ± 21	< .001
Hemoglobin, g/dL	13.6 ± 1.8	13.7 ± 1.7	12.5 ± 1.8	< .001
Biological valve prosthesis	5 (0.5)	4 (0.5)	1 (1.0)	.488
Significant valve disease[c]	168 (18.7)	136 (16.9)	32 (34.8)	< .001
Mitral regurgitation	109 (12.2)	87 (10.8)	22 (23.9)	< .001
Aortic stenosis	39 (4.3)	31 (3.9)	8 (8.7)	.031
Aortic regurgitation	44 (4.9)	37 (4.6)	7 (7.6)	.206
LVEF ≤ 50%	97 (11.3)	79 (10.2)	18 (20.9)	.003
Pharmacological treatment				
ASA	84 (8.6)	70 (8.1)	14 (13.7)	.054
Antiplatelet therapy	92 (9.4)	75 (8.6)	17 (16.7)	.009
Prior VKA	377 (38.8)	323 (37.3)	53 (52)	.004
Beta-blockers	541 (55.6)	476 (54.8)	63 (61.8)	.179
ACEI/ARA-II	641 (65.9)	577 (66.4)	63 (61.8)	.350
Aldosterone antagonists	66 (6.8)	49 (5.6)	17 (16.7)	< .001
Loop diuretics	315 (32.4)	258 (29.7)	57 (55.9)	< .001
Rivaroxaban	505 (52.0)	456 (52.5)	49 (52)	
Dabigatran	188 (19.3)	165 (19.0)	22 (21.6)	.680
Apixaban	280 (28.7)	248 (28.5)	31 (30.4)	

ACEI, angiotensin converting enzyme inhibitor; AF, atrial fibrillation; ASA, acetylsalicylic acid; ARA-II, angiotensin II receptor antagonist; $CHADS_2$, Heart failure, hypertension, age > 90 years, diabetes mellitus, and Stroke (double); CHA_2DS_2VASc, Heart failure, hypertension, age ≥ 65 years [double], diabetes mellitus, stroke (double); CKD-EP, Chronic Kidney Disease Epidemiology Collaboration; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; HAS-BLED, hypertension, abnormal renal/liver function, stroke, history or predisposition to bleeding, INR lability, age > 65 years, and concomitant medication or alcohol; INR, international normalized ratio; LVEF, left ventricular ejection fraction; TIA, transient ischemic attack; VKA, vitamin K antagonist.
Data expressed as mean ± SD or No. (%).
[a] Chronic renal disease is defined as GFR estimated by CKD-EPI < 60 mL/min/1.73 m^2.
[b] Percentage relative to patients with a history of VKA use.
[c] Moderate-severe valve disease.

Table 2
Multivariate Analysis of Cox Proportional Risks for Prediction of Overall, Cardiovascular, and Noncardiovascular Death

	Overall mortality		Cardiovascular death		Noncardiovascular death	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Diabetes mellitus	1.71 (1.13-2.59)	.011				
Ischemic heart disease	1.89 (1.11-3.22)	.020				
Significant valve disease	1.72 (1.08-2.75)	.023	2.40 (1.12-5.13)	.024		
Female sex			0.43 (0.20-0.90)	.025		
GFR (CKD-EPI) (× mL/min/1.73 m^2)			0.97 (0.95-0.99)	.005	1.02 (1.00-1.04)	0.022
Hemoglobin (× g/dL)	0.79 (0.69-0.89)	< .001	0.81 (0.66-0.99)	.035	0.73 (0.61-0.87)	< .001
Heart failure	2.90 (1.80-4.68)	< .001	3.28 (1.46-7.40)	.004	3.23 (1.69-6.18)	< .001
Prior neoplasm	3.34 (1.99-5.59)	< .001			3.95 (2.04-7.63)	< .001
Age (× y)	1.07 (1.04-1.11)	< .001			1.11 (1.05-1.17)	< .001
COPD and/or asthma					2.00 (1.06-3.71)	0.032

CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; chronic obstructive pulmonary disease; GFR, glomerular filtration rate; HR, hazard ratio; 95% CI, 95% confidence interval; TIA, transient ischemic attack.
Multivariate model adjusted for age, sex, persistent-permanent AF, diabetes mellitus, COPD and/or asthma, stroke and/or prior TIA, ischemic heart disease, peripheral artery disease, heart failure, neoplasm, previous major bleeding, GFR estimated according to CKD-EPI, hemoglobin, significant valve disease, left ventricular ejection fraction, and direct-acting oral anticoagulant received.

for death in these patients in order to improve planning of strategies to increase survival. As shown above, this study identified as predictors risk markers such as age and sex on the one hand and modifiable risk factors such as diabetes mellitus, ischemic heart disease, heart failure, neoplasms, renal failure, anemia, chronic obstructive pulmonary disease, and valve diseases, on the other. These modifiable risk factors can be targeted with preventive and therapeutic measures. Therefore, the main objectives should be to improve cardiovascular risk factor control and achieve adherence to the recommendations of clinical

practice guidelines for the management of concurrent diseases associated with atrial fibrillation.[4] Finally, the main limitations of this study are its retrospective design and the absence of a control group, as they prevent us from knowing for certain whether the observed increased mortality occurs in all patients with NVAF regardless of the anticoagulant prescribed or whether DAOA therapy somehow selects patients at higher risk.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found in the online version available at http://dx.doi.org/10.1016/j.rec.2017.03.032.

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REFERENCES

1. Gómez-Outes A, Lagunar-Ruíz J, Terleira-Fernández A-I, Calvo-Rojas G, Suárez-Gea ML, Vargas-Castrillón E. Causes of death in anticoagulated patients with atrial fibrillation. *J Am Coll Cardiol.* 2016;68:2508–2521.
2. Olesen JB, Sørensen R, Hansen ML, et al. Non-vitamin K antagonist oral anticoagulation agents in anticoagulant naïve atrial fibrillation patients: Danish nationwide descriptive data 2011-2013. *Europace.* 2015;17:187–193.
3. Moreno-Arribas J, Bertomeu-González V, Anguita-Sanchez M, et al. Choice of new oral anticoagulant agents versus vitamin k antagonists in atrial fibrillation: FANTASIIA Study. *J Cardiovasc Pharmacol Ther.* 2016;21:150–156.
4. Arribas F, Roldán I, Luis Merino J, et al. Comentarios a la guía ESC 2016 sobre el diagnóstico y tratamiento de la fibrilación auricular. *Rev Esp Cardiol.* 2017;70:2–8.

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Acute Myocarditis Versus Ventricular Noncompaction Cardiomyopathy in Infancy: Role of Magnetic Resonance

Miocarditis aguda frente a miocardiopatía no compactada en el lactante: utilidad de la resonancia magnética

To the Editor,

Acute myocarditis is an inflammatory process affecting the myocardium that mainly occurs secondary to a viral infection. The definitive diagnosis is established by endomyocardial biopsy,[1] but because this method is invasive, it is performed only in selected patients. A presumptive diagnosis can be reached by taking a clinical history and performing noninvasive complementary tests.[1,2] Among these, cardiac magnetic resonance (CMR) imaging plays an important role, and experience with this technique is increasing in children.[3] CMR can detect the tissue changes inherent to myocarditis, such as edema, hyperemia, and necrosis. To establish the diagnosis, at least 2 of the 3 CMR criteria must be fulfilled.[4] The sensitivity of the test varies according to the clinical pattern: sensitivity is very high in the forms presenting with precordial pain, but is lower in patients with dilatation and ventricular dysfunction. In these patients, the differential diagnosis should be made with other conditions such as dilated cardiomyopathy or noncompaction cardiomyopathy. This latter disease can present with a pattern of heart failure at any age, and the diagnosis is established on the basis of echocardiographic[5] and CMR[6] criteria.

We present a series of 3 patients admitted to our center between April 2015 and September 2016 with clinical signs and symptoms of cardiogenic shock. The patients' characteristics are described in Table. All required inotropic support and mechanical ventilation. After they had been stabilized, the patients were extubated, and standard heart failure therapy was initiated. The first 2 patients had experienced an infectious process before symptom onset. At admittance they underwent electrocardiography, echocardiography, blood analysis to determine myocardial injury markers, and polymerase chain reaction (PCR) testing for cardiotropic viruses in blood and respiratory secretions. CMR was performed during the first 3 days following admittance, with the patients under sedation and breathing spontaneously. Only 1 patient tested PCR-positive in a blood sample, with detection of parvovirus B19 (Table). All 3 patients had left ventricular dilatation and hypertrabeculation, and they met the diagnostic criteria of noncompaction cardiomyopathy both on CMR and echocardiography.[5,6] There was a good correlation between the ejection fraction determined by CMR and the estimated value obtained with the Teichholz formula on echocardiography (Table). A hyperintense signal on CMR T_2 sequences and increased early gadolinium uptake were seen in all patients. Of note, both the hyperintensity and signal increase in the early phase following gadolinium administration were localized at the trabeculated region, but did not reach the compacted myocardium (Figure). In the second and third patient, the right ventricle also showed considerable trabeculation. In the first patient, who tested PCR-positive for parvovirus B19 in blood and had a poor clinical course, endomyocardial biopsy was carried out. The results were normal, and diagnosis of acute myocarditis was ruled out. Thus, the diagnostic orientation in the 3 patients was noncompaction cardiomyopathy with severe ventricular dysfunction.

At the time of writing, the 3 patients have been stable, show moderate-severe ventricular dysfunction, and are receiving heart failure treatment.

In conclusion, we wish to convey the usefulness of CMR for the etiological diagnosis of ventricular dysfunction in pediatric patients. This technique should be among the first to be used in these patients, as it can avoid the need for invasive examinations that are not without risk, such as endomyocardial biopsy. This procedure should be carried out in selected patients, particularly in the pediatric population. In infants with noncompaction cardiomyopathy and severe left ventricular dysfunction, the differential diagnosis with acute myocarditis can be challenging. Trabeculation appears hyperintense on T_2 images and slow flow due to severe