The 2 risk charts thus show a satisfactory level of agreement by intraclass correlation coefficient and kappa statistic (except for women); however, cardiovascular risk was systematically lower on the SCORE OP chart. European guidelines recommend a more cautious pharmacological approach with patients older than 60 years because the calculated risk can be high simply due to the patient’s age, even when no other risk factors are present.

In Spain, 2 risk charts have been generated from direct analysis of the Spanish population, including the elderly population: the ERICE study, which includes participants ranging in age from 30 years to more than 80 years,7 and the FRESCO study, which includes individuals aged from 35 to 79 years.8 These risk calculations are awaiting external validation of their usefulness and impact compared with already available risk charts.

A limitation of the present study is the incomplete dataset for SBP and TC, which impeded risk calculation for some patients. Another limitation is that the analysis was restricted to primary care patients, raising uncertainties about whether the results can be extrapolated to the general population.

Among people older than 65 years, the SCORE OP risk chart gives lower cardiovascular risk estimates than the original SCORE chart, suggesting that fewer patients in this age group might benefit from statin therapy than previously thought. Further validation studies of these risk charts are needed in the Spanish population to assess the level of discrimination and calibration.

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**REFERENCES**


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The complete methodology of this population-based cross-sectional study entirely conducted in the province of Badajoz (Extremadura; southwest Spain) has been published elsewhere.1 Of 2833 participants, 135 were excluded due to previous cardiovascular event (ie, myocardial infarction, angina, or stroke). A total of 2698 participants (aged 25–79 years) were finally included.

Age, educational and occupational status, smoking and alcohol consumption were registered through personal interview. Systolic and diastolic blood pressures were measured according to the European Society of Hypertension. Resting heart rate was measured from the radial pulse for 30 seconds. Plasma insulin, apolipoproteins A and B, high-sensitivity C-reactive protein, glycosylated hemoglobin, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, total cholesterol, glucose, urea, albumin, creatinine, and fibrinogen concentrations were measured by standard procedures. The albumin–creatinine ratio and estimated glomerular filtration rate were also determined.

Leisure time PA was self-reported through the Minnesota Leisure Time Physical Activity Questionnaire. Participants were classified as physically active if they met the PA guidelines (ie, total PA energy expenditure ≥ 500 metabolic equivalents per week).

We defined metabolically healthy or unhealthy in accordance with the Consensus Societies for the definition of metabolic syndrome, and classified individuals into 4 body-size phenotype (ie, obese or nonobese, metabolically healthy or unhealthy).
Glycemic profile

- Fasting glucose, mg/dL: 95.6 ± 0.66\(^{ab}\) vs 111.3 ± 0.97\(^{ac}\) vs 98.4 ± 1.19\(^{ab}\) vs 115.2 ± 0.94\(^{bc}\) \(<.001\)
- Fasting insulin, mg/dL: 6.40 ± 0.18\(^{ab}\) vs 10.1 ± 0.27\(^{cd}\) vs 10.7 ± 0.33\(^{bc}\) vs 15.2 ± 0.26\(^{ab}\) \(<.001\)
- HOMA-IR: 1.54 ± 0.09\(^{ab}\) vs 2.87 ± 0.11\(^{cd}\) vs 2.64 ± 0.14\(^{bc}\) vs 4.48 ± 0.11\(^{ab}\) \(<.001\)
- Glycosylated hemoglobin, n (%): 4.97 (0.22)\(^{ab}\) vs 5.31 (0.03)\(^{cd}\) vs 5.07 (0.09)\(^{bc}\) vs 5.46 (0.03)\(^{ab}\) \(<.001\)
- Diabetes (≥ 126 mg/dL), n (%): 18 (1.5)\(^{ab}\) vs 99 (18.3)\(^{ab}\) vs 21 (6.3)\(^{bc}\) vs 156 (26.9)\(^{ab}\) \(<.001\)

Vascular function

- Heart rate, bpm: 70.3 ± 0.33\(^{ab}\) vs 73.9 ± 0.49\(^{bc}\) vs 71.5 ± 0.60\(^{bc}\) vs 74.8 ± 0.48\(^{bc}\) \(<.001\)
- Systolic blood pressure, mmHg: 117.3 ± 0.45\(^{ab}\) vs 129.0 ± 0.66\(^{bc}\) vs 121.1 ± 0.81\(^{bc}\) vs 130.9 ± 0.64\(^{bc}\) \(<.001\)
- Diastolic blood pressure, mmHg: 70.2 ± 0.26\(^{ab}\) vs 76.6 ± 0.41\(^{bc}\) vs 75.4 ± 0.51\(^{bc}\) vs 79.5 ± 0.40\(^{bc}\) \(<.001\)
- Hypertension (≥ 140/90 mmHg), n (%): 96 (7.7)\(^{ab}\) vs 252 (46.5)\(^{cd}\) vs 57 (17.2)\(^{bcd}\) vs 323 (55.7)\(^{bcd}\) \(<.001\)
- Between-arms SBP diff., mm/Hg: 0.52 ± 0.25\(^{ab}\) vs 1.71 ± 0.37\(^{cd}\) vs 1.59 ± 0.46\(^{bc}\) vs 1.88 ± 0.36\(^{bc}\) \(<.01\)
- Pulse pressure, mmHg: 47.9 ± 0.37\(^{ab}\) vs 53.4 ± 0.54\(^{bcd}\) vs 46.7 ± 0.66\(^{bc}\) vs 52.5 ± 0.52\(^{bcd}\) \(<.001\)
- Pulse pressure > 50 mmHg, %: 253 (20.4)\(^{ab}\) vs 325 (60.0)\(^{bcd}\) vs 101 (30.4)\(^{bcd}\) vs 353 (60.9)\(^{bcd}\) \(<.001\)
- Ankle-brachial index, mmHg: 1.09 ± 0.004\(^{ab}\) vs 1.07 ± 0.005\(^{ab}\) vs 1.07 ± 0.006\(^{ab}\) vs 1.07 ± 0.005\(^{ab}\) \(<.001\)
- Ankle-brachial index < 90 n (%): 16 (1.3)\(^{ab}\) vs 24 (4.4)\(^{ab}\) vs 10 (3.0)\(^{ab}\) vs 29 (5.0)\(^{ab}\) \(<.001\)

Renal function

- Urea, mg/dL: 36.8 ± 0.30 vs 36.8 ± 0.43 vs 37.8 ± 0.53 vs 37.9 ± 0.42 \(0.085\)
- Creatinine, mg/dL: 0.82 ± 0.06 vs 0.84 ± 0.008 vs 0.83 ± 0.010 vs 0.85 ± 0.008 \(0.066\)
- Albumin-creatinine ratio: 7.21 ± 2.78\(^{ab}\) vs 17.9 ± 4.11 vs 5.26 ± 5.04\(^{bc}\) vs 22.36 ± 3.98\(^{bc}\) \(0.008\)
- Abnormal urinary albumin excretion, n (%): 28 (2.3)\(^{ab}\) vs 34 (6.3)\(^{ab}\) vs 12 (3.6)\(^{ab}\) vs 56 (9.7)\(^{ab}\) \(0.001\)
- Glomerular filtration rate, ml/min/m\(^2\): 94.8 ± 0.57 vs 94.1 ± 0.83 vs 93.2 ± 1.03 vs 92.7 ± 0.81 \(0.163\)
- Glomerular filtration rate < 60 ml/min, n (%): 17 (1.4)\(^{abcd}\) vs 27 (5.0)\(^{ab}\) vs 17 (6.6)\(^{ab}\) vs 38 (7.3)\(^{ab}\) \(0.001\)

Physical activity

- MVPA (≥ 4 METs), METs/wk: 226.6 ± 9.5\(^{a}\) vs 182.5 ± 14.0 vs 181.7 ± 17.3 vs 141.2 ±13.6\(^{a}\) \(0.001\)
- Total expenditure (excluding domestic PA), METs/wk: 282.6 ± 8.1\(^{ab}\) vs 235.6 ± 12.0\(^{cd}\) vs 234.8 ± 14.7\(^{bc}\) vs 187.9 ± 11.6\(^{bc}\) \(0.001\)
- Total expenditure (including domestic PA), METs/wk: 593.1 ± 11.7\(^{ab}\) vs 450.0 ± 17.2\(^{bc}\) vs 548.2 ± 20.7\(^{cd}\) vs 418.4 ± 16.3\(^{bc}\) \(0.001\)
- Meet PA guidelines (including domestic PA), n (%): 651 (52.5)\(^{ab}\) vs 197 (36.3)\(^{ab}\) vs 159 (47.9)\(^{cd}\) vs 199 (34.3)\(^{bc}\) \(0.001\)
- Low intensity (< 3 METs), METs/wk: 65.4 ± 2.9 vs 59.9 ± 4.2 vs 56.3 ± 5.2 vs 52.2 ± 4.1 \(0.066\)
- Medium intensity (3.0-6.0 METs), METs/wk: 126.8 ± 7.6\(^{a}\) vs 97.8 ± 11.2 vs 96.1 ± 13.8 vs 72.1 ± 10.9\(^{a}\) \(0.001\)
- High intensity (> 6 METs), METs/wk: 99.8 ± 5.6\(^{a}\) vs 84.8 ± 8 vs 85.7 ± 10.2 vs 69.1 ± 8.0\(^{a}\) \(0.030\)

Apo A, apolipoprotein A; Apo B, apolipoprotein B; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; LDL-C, low-density lipoprotein cholesterol; PA, physical activity; MET, metabolic equivalent of task; MVPA, moderate-vigorous physical activity; SBP, systolic blood pressure; wk, week. 1MET = 3.5 ml of oxygen uptake/kg/min.

Values shown as mean ± standard error unless otherwise indicated; analyses were performed with ANCOVA with age, sex, smoking (yes/no), alcohol consumption (mL) and educational status as covaribles; upper case letters/letters in the same row indicates a significant pairwise difference \(P < .05\) between groups with the same letter. The Bonferroni correction for multiple comparisons was applied to analyze pairwise differences.
Obesity was defined as body mass index $\geq 30$ kg/m² and waist circumference was excluded from the criteria.

One-way analysis of covariance (ANCOVA) was used to assess the differences in cardiometabolic markers across body-size phenotypes after adjustment for age, sex, smoking, alcohol consumption, and educational status. Sex differences were assessed using ANCOVA with the aforementioned covariates. The Bonferroni correction for multiple comparisons was applied.

The prevalence of MHO was 12% (36% among the obese). Women had a higher prevalence of MHO (15% vs 10%, respectively) and metabolically healthy nonobese (71% vs 44%) phenotypes than men (both $P < .001$, Table and Figure 1 of the supplementary material). Men had a more impaired cardiometabolic profile and lower PA levels than women (all $P < .001$, Table and Figure 2 of the supplementary material). Despite the expectable differences in traditional markers of metabolic syndrome, the MHO group was younger and had higher plasma apolipoprotein A and lower triglycerides, low-density lipoprotein cholesterol, glycosylated hemoglobin, resting heart rate and pulse pressure than both metabolically unhealthy obese and nonobese (Table and Figure). The inflammatory profile was more impaired in all the groups in comparison to the metabolically healthy nonobese (Table). The MHO group had a more favorable renal profile (lower prevalence of abnormal urinary albumin excretion and albumin-creatinine ratio) than the metabolically unhealthy obese (Table). Finally, the obese and the metabolically unhealthy groups showed lower total energy expenditure in PA and less fulfillment of the PA recommendations than the MHO group ($P < .001$, Table).

The MHO participants showed higher levels of all-type PA and a higher proportion of individuals meeting the PA guidelines than metabolically unhealthy obese. Other studies revealed that MHO individuals spend less time in sedentary behavior and more time in light PA and active commuting than metabolically unhealthy obese.

A major finding of this study is that women had higher PA levels (especially when domestic PA was accounted for) and this could partially explain the higher proportion of MHO observed among women. Similarly, the higher PA levels observed among

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**Figure.** Clustered (z-score) adverse lipid profile (A), glycemic profile (B), vascular function (C) and renal function (D) by phenotype groups and sex. Dots represent mean ± standard error. Letters indicate a pairwise significant difference ($P < .05$) for each sex between phenotype groups with the same letter. The model (1-way analysis of covariance) was adjusted for age, educational status, smoking, and alcohol consumption. Pairwise comparisons were performed with Bonferroni’s adjustment. Adverse lipid profile consisted of the standardized scores [\(\text{value-mean}/\text{standard deviation}\)] of plasma triglycerides, LDL–C, Apo B and inverted HDL–C and Apo A (A). Adverse glycemic profile consisted of fasting glucose, insulin and glycosylated hemoglobin (B). Adverse vascular profile consisted of resting heart rate, systolic and diastolic blood pressure (C). Adverse renal profile comprised plasma urea and creatinine and urinary microalbumin and inverted glomerular filtration rate (D). Apo A, apolipoprotein A; Apo B, apolipoprotein B; HDL–C, high-density lipoprotein cholesterol; LDL–C, low-density lipoprotein cholesterol.
women could partly explain the more favorable cardiometabolic profile observed in women regardless of the body-size phenotype. Indeed, most women were housewives and they spent 10 times more energy in domestic PA than men, which could imply a substantial reduction in cardiometabolic risk. This hypothesis is supported by previous studies reporting that light household PA is associated with lower cardiovascular and all-cause mortality.

Our results reinforce the idea that PA might play an important role on the MHO phenotype and its prognosis. The cross-sectional design and lack of objective assessment of PA, physical fitness, fatness and nutritional patterns are limitations of this study that should be considered in future studies. Since low PA is a common feature of the metabolically unhealthy obese phenotype, PA or exercise programs could play an important role in this population. In addition, further research is needed to determine whether increasing PA among MHO individuals might prevent the transition from MHO to a metabolically unhealthy state or promote the opposite, which has been previously reported to occur.

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SUPPLEMENTARY MATERIAL
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Structural Heart Disease in Anticoagulated Patients With Nonvalvular Atrial Fibrillation: Prevalence and Clinical Profile in a Spanish Sample

Cardiopatía estructural en pacientes anticoagulados con fibrilación auricular no valvular: prevalencia y perfil clínico en una muestra nacional

To the Editor,

Although the definition of nonvalvular atrial fibrillation (NVAF) varies,1,2 it generally does not exclude patients with structural heart disease (SHD), such as certain valve diseases. However, there is limited information on the frequency of this association in Spain. The objective of this article was to report the prevalence and clinical profile of patients with SHD and well as the prevalence of heart failure in a broad Spanish nationwide sample of patients with NVAF.

Data from the FANTASIIA registry3 were used. This registry included 2178 outpatients with NVAF who were receiving anticoagulation (according to protocol, the ratio of vitamin K antagonists to direct anticoagulants was 4:1). We excluded individuals younger than 18 years, those with prosthetic cardiac devices, those with any grade of mitral stenosis, and those with moderate or severe mitral regurgitation. Participants were enrolled consecutively between June 1, 2013, and October 15, 2014, in 50 Spanish centers selected by the investigators to ensure representation from throughout the country, with the primary objective of assessing the effectiveness of anticoagulation in patients with NVAF by type and quality of treatment. The diagnoses of SHD were taken from the medical records and included the following: coronary artery disease, hypertensive heart disease, dilated cardiomyopathy, hypertrophic cardiomyopathy, significant valve disease (aortic valve, tricuspid valve, or pulmonary valve disease of at least moderate intensity), and other heart diseases. Patients with coronary artery diseases and other concurrent heart diseases were classified as having coronary artery disease. The presence of heart failure was recorded independently. Overall, 47.15% of the sample had SHD (Table 1). The most frequent type of SHD was coronary artery disease (18.14%), followed by hypertensive heart disease (11.43%), and dilated cardiomyopathy (6.01%). Hypertrophic cardiomyopathy was reported in 2.06% and significant valve diseases in 1.79%. Only 34 patients (1.56%) had isolated NVAF (age < 65 years, with no heart disease or embolic risk factor). Among patients with SHD, there were fewer


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REFERENCES