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Assessment of HARMS2-AF for risk stratification: a 10-year follow-up study (2014–2024) in a northwestern Colombian population

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Introduction: Atrial fibrillation (AF) is the most prevalent arrhythmia worldwide and represents a significant public health burden. Several modifiable risk factors (RFs) — such as hypertension, obesity, smoking, alcohol consumption, sleep apnea, and physical inactivity — contribute to its development. However, their combined effect has not been thoroughly assessed in Latin American populations.

Objective: to develop and validate the HARMS2-AF model to predict AF risk based on modifiable RFs, assessing its applicability in primary care settings.

Materials and Methods: an observational retrospective cohort study was conducted with 2,482 participants from Northwestern Colombia, followed over 10 years. RFs evaluated included hypertension, obesity (BMI ≥30 kg/m^2), smoking, alcohol consumption (≥15 standard drinks/week), sleep apnea, physical inactivity, diabetes mellitus, age, and sex. Cox proportional hazards regression models (univariate and multivariate) were used to generate HARMS2-AF scores based on beta coefficients. Model performance was assessed using the area under the receiver operating characteristic curve (AUC) and calibration tests.

Results: hypertension was the most prevalent RF (79.1%) and the strongest predictor of AF (HR 4.0; 95% CI: 3.2–4.8). Obesity, high alcohol intake, smoking, and sleep apnea were also significantly associated with AF. Physical inactivity and diabetes mellitus did not reach statistical significance in multivariate analysis. The HARMS2-AF model showed a two-fold increase in AF risk per 1-point increment (HR 2.38; 95% CI: 2.14–2.62), with an AUC of 0.81.

Conclusion: the HARMS2-AF model is a simple and effective tool for predicting AF risk based on modifiable RFs. Its implementation in primary care could enhance early identification and targeted prevention strategies in Latin American populations.

INTRODUCTION

Atrial fibrillation (AF) is the most prevalent arrhythmia at world level, representing a significant challenge in terms of clinical and economic load.[1] Historically, AF has been closely related with traditional risk factors, many of which are partially modifiable or nonmodifiable, such as hypertension, diabetes mellitus and heart failure. However, advancements in therapeutic strategies, such as catheter ablation and thromboembolic risk prevention with new oral anticoagulants, have substantially improved AF treatment and outcome.

More recently, factors related with lifestyle have been identified as the "fourth pillar" in AF treatment, highlighting their modifiable potential as an opportunity for early directed interventions.[2] Among the modifiable risk factors of AF we have obesity, sleep apnea, alcohol consumption and smoking. The specific interventions about these factors have shown a significant reduction in the incidence and recurrence of AF. For instance, a clinical study showed that the reduction or abstinence of alcohol consumption substantially decreased the incidence of AF.[3] Moreover, clinics focused on risk factor modification have promoted strategies such as weight loss, increase in physical activity and control of cardiovascular risk factors, with positive effects on the secondary prevention of AF, particularly after ablation.[4,5]

Nevertheless, it hasn't been determined yet to what extent each lifestyle factor contributes to the individual risk of developing AF, nor how the coexistence of multiple modifiable factors affects this risk.[6] Although risk prediction models for AF detection in the general population are used increasingly, these are predominantly focused on traditional factors, mainly nonmodifiable ones, leaving a significant gap in the inclusion of lifestyle factors.[7,8,9,10]

In this study, we aim to evaluate the usefulness of the HARMS2-AF score, a tool previously developed and vali-

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dated by Segan et al (2023), integrating modifiable risk factors into AF prediction. Through a retrospective analysis of a north-western cohort of Colombia, we attempted to determine its applicability in a Latin American environment, and to explore its value to identify individuals in higher risk of AF, facilitating personalized interventions for prevention.

MATERIALS AND METHODS

Design of the study and population context

This is a retrospective, observational and cohort study, designed to evaluate the applicability of the HARMS2-AF score in a north-western cohort of Colombia, followed over a period of 10 years (2014-2024). The participants belong to an institutional program of cardiovascular prevention, with regular medical care and digitized clinical records within a network of centers that allow obtaining most clinical events.

Data sources

Data were extracted from institutional electronic clinical histories, including socio-demographic variables, medical history, diagnoses codified by ICD-10, laboratory test results and clinical course documented by family doctors and specialists.

Eligibility criteria

- Inclusion:
  - Patients ≥18 years at the time of admission.
  - Members of the cardiovascular prevention program with active follow-up for at least 12 months.
  - Availability of complete clinical information for the estimation of the HARMS2-AF score.
  - With no previous diagnosis of atrial fibrillation.
- Exclusion:
  - Diagnosis of atrial fibrillation before admission.
  - Incomplete clinical records or essential information missing.
  - Less than one year of follow-up.

Evaluation of predictors

The risk factors included in the model were: smoking, alcohol consumption, physical inactivity, body mass index (BMI), sleep apnea, type 2 diabetes mellitus, hypertension, age and sex.

- Modifiable factors:
  - *Smoking:* classified as current, previous or non-smoker.
  - *Alcohol consumption:* low (≤standard drinks/week), moderate (7-14) and high (≥15).
  - *Physical inactivity:* defined as <600 MET-min/week, according to IPAQ.
  - *BMI:* obesity defined as ≥30 kg/m2.
- Non-modifiable factors:
  - *Age:* <60 years (0 points), 60-64 (1 point), ≥65 (2 points).
  - *Male gender:* 1 point.

TABLE 1.
HARMS2-AF score criteria.

Criterion	Score
Hypertension	4 points
Age 60–64 years	1 point
Age ≥65 years	2 points
BMI ≥30 kg/m²	1 point
Male gender	1 point
Sleep apnea	1 point
Smoking	1 point
Alcohol consumption (7–14/week)	1 point
alcohol consumption (≥15/week)	2 points

TABLE 2.
Main comorbidities of patients included in the study.

Variable	N values
Hypertension	1963 / 2482
Diabetes mellitus not requiring insulin	751 / 2482
Diabetes mellitus requiring insulin	178 / 2482
Abdominal obesity	458 / 2482
Hypercholesterolemia, low HDL	680 / 2482
Chronic obstructive pulmonary disease	100 / 2482
Hypertriglyceridemia	502 / 2482
Sleep apnea	189/2482
Smoking	457/2482
Alcohol consumption between 7-14	385/2482
Alcohol consumption of more than 15	203/2482

- Comorbidities:
  - *Hypertension, type 2 diabetes and sleep apnea:* diagnosed by clinical history, pharmacological treatment or ICD-10 codes.
  - *ICD-10 codes used:*
    - AF: I48.x
    - Hypertension: I10–I15
    - Type 2 diabetes: E11.x
    - Sleep apnea: G47.3.

Evaluation of results

The primary outcome was the time until the first diagnosis of atrial fibrillation, defined as:

- Event documented in institutional medical records.
- Codification with ICD-10: I48.x
- Diagnosis confirmed by attending physician or specialist.

Statistical analysis

- Continuous variables are described as mean±standard deviation or median (IQR), according to distribution. Categorical variables are expressed in absolute frequencies and percentages.

- Univariate Cox regression analysis was used to explore individual associations.
- The variables with statistical significance ($p<0.05$) were included into a multivariate model to assess independent predictors of AF.
- Beta coefficients of the multivariate model were not recalibrated; the original HARMS2-AF structure was used.

Risk stratification

- Low risk: 1-4 points
- Intermediate risk: 5-9 points
- High risk: 10-14 points.

Model validation

The model was evaluated by:

- Area under the ROC curve (AUC) for a 10-year discrimination.
- Calibration curves comparing observed vs expected events.
- Hazard ratio (HR) estimation for each additional point in the score.

Ethical considerations

This study was approved by the Institutional Ethics Committee. It was guaranteed that all principles of the Declaration of Helsinki were met, as well as the national regulations on biomedical investigation.

RESULTS

Sociodemographic characterization

The population studied was made up by 2482 patients, with a predominant distribution of the female gender (1369 patients, 55.2%) in comparison with the male gender (1113 patients, 44.8%). The average age of the participants was 67.9 years, reflecting a mainly adult and advanced age population.

As to access to specialized health services, 5.4% of patients (135/2482) received a psychological assessment, while most, 84.9% (2109/2482) had access to a nutritional evaluation. Besides, 28.3% of patients (702/2482) received odontological care.

The incidence of AF was lower in patients with high therapeutic adherence, with a HR of 1.86 (95% CI: 1.62-2.15) in comparison with those with low adherence.

These data reflect both the sociodemographic characteristics and the pattern of access to health care services of the population included in the study, offering an initial view on the scenario within which the rest of the clinical evaluations were carried out.

In *Table 3,* the data corresponding to adherence, degree of control and means of the values of lipid profile, renal function and glucose of patients are presented.

The mean time until the first event of AF was 4.8 years (SD±2.1), with a median of 4.6 years (IQR: 3.2-6.3), displaying a gradual progression of risk in this cohort, showing a significant increase in risk of AF per each point increase in the general HARMS2-AF score [HR 2.38 (95% CI: 2.14-2.62)]. Furthermore, an incremental risk of AF was observed according to the categories of stratified risk by the score, emphasizing its usefulness as a predictive tool in this population.

TABLE 3.
Adherence, degree of control, means of lipid profile, glucose and renal function of patients.

Variable	Value
Patients with good therapeutic adherence	1205 (48.5%)
Patients with appropriate control	1104 (44.5%)
Total cholesterol (mg/dl)	197.48
HDL (mg/dl)	40.86
LDL (mg/dl)	135.72
TRIGLYCERIDES (MG/DL)	205.85
Fasting glucose (mg/dl)	108.3
HBA1C (%)	6.8
GFR test (ml/min/1.73 m²)	72.5

DISCUSSION

This study evaluated the impact of modifiable risk factors (RF) on atrial fibrillation (AF) during a 10-year follow-up in a north-western population of Colombia, developing and validating the HARMS2-AF prediction model. The findings reaffirm the clinical relevance of modifiable RFs and underscore the need to incorporate these factors into clinical practice for the prevention and management of AF.[11,12]

Hypertension emerged as the strongest independent risk factor, with a risk almost four times higher of incident AF; results that coincide with previous studies highlighting the direct association between elevated high pressure and the development of AF. Obesity and sleep apnea also showed a strong relationship with AF. BMI ≥30 kg/m2 significantly increased risk, while sleep apnea was an independent predictor, even after adjusting for other RFs. These findings reinforce the need for specific strategies to control these conditions in the general population and in primary care.[13,14]

Alcohol consumption showed a dose-dependent relationship with AF incidence, particularly in those consuming ≥15 standard drinks per week. This adverse effect is consistent with studies that have linked the chronic consumption of alcohol with atrial enlargement and low tissue voltage. Although smoking was also associated with a higher risk, data suggest that early interventions in these factors may reduce the incidence of AF. [15,16]

Physical inactivity and diabetes mellitus, although associated to incident AF in univariate analysis, did not reach significance in multivariate analysis. These could be attributed to biases in the measurement of self-reported physical activity or the lack of detailed information on intolerance to carbohydrates in relation to diabetes.[17]

The HARMS2-AF model is the first in Latin America prioritizing modifiable RFs in the prediction of risk of AF. It is a simple tool, that does not depend on complex diagnostic tests and can be used both at the patient's bedside and in population screenings. However, this model requires validation in wider and more diverse populations to confirm its widespread applicability.[18]

Adherence to treatment emerged as a significant modulator of AF risk, suggesting that follow-up and therapeutic education strategies may play a key role in the reduction of incident events.

The results suggest that a HARMS2-AF score of ≥5 should trigger aggressive interventions to modify RFs and reduce the risk of AF. Besides, the model emphasizes the importance of preventive strategies in primary care, where communication about risks and the prioritization of treatments may play a key role in the prevention of AF and its complications.[12,19]

Limitations of the study

Self-reported data for some risk factors:

Physical activity and alcohol consumption were based on self-report questionnaires, which may induce memory biases and under or overestimate their impact on the risk of atrial fibrillation (AF).

Lack of electrocardiographic and echocardiographic data:

The HARMS2-AF model does not include parameters such as atrial dilatation or cardiac electrical activity, which may improve accuracy in risk prediction.

Underestimation of asymptomatic AF:

AF detection was based on medical and in-hospital records, which probably excluded asymptomatic or undiagnosed cases, limiting the true incidence reported.

Predominantly Latin American population:

Although this is a strong point for the region, the findings may be not translatable to populations with a different ethnical or socioeconomic composition.

Simplified categories of continuous variables:

Variables such as age, body mass index and alcohol consumption are categorized in clinical thresholds to facilitate the applicability of the model, but this may miss significant details in nonlinear relationships between these factors and AF.

Besides the diagnosis of atrial fibrillation, other major cardiovascular events were documented, such as acute myocardial infarction and ischemic stroke, when such information was available in the institutional records.

It was not possible to systematically capture all major cardiovascular outcomes, which represents a methodological limitation. Their inclusion is advised in future validations, to evaluate the comprehensive impact on risk factors.

Additionally, this study did not include electrocardiographic or echocardiographic variables, widely acknowledged as essential in the evaluation of AF risk. The absence of data on interatrial block, an electrocardiographic finding easy to obtain by 12-lead ECG and related with atrial remodeling and risk of arrhythmia, is a relevant omission. Likewise, no measurements were added to the size of the left atrium, which reflect chronic structural changes predisposing to the development and perpetuation of AF, and may be easily obtained through transthoracic echocardiography. Numerous studies have shown that interatrial block and left atrial dilatation not only predict the appearance of AF, but are also associated with a worse clinical outcome, including post-ablation relapse and greater risk of embolic events. Their exclusion in the HARMS2-AF model limits the capacity for a comprehensive stratification of risk, by dispensing with anatomical and functional components reflecting the underlying arrhythmogenic substrate. In this regard, although the model is focused on modifiable factors, easily assessed in primary care, the integration of these markers may offer an added value in scenarios where basic diagnostic tools are available, improving the accuracy of the model, not compromising its applicability. We emphatically recommend considering their inclusion in future versions of the score, and in external validation studies that would allow evaluating their impact on the prediction and prevention of AF in a stronger manner.

CONCLUSION

The HARMS2-AF model has proven to be a useful tool to predict the risk of atrial fibrillation based on modifiable lifestyle factors, such as hypertension, obesity, alcohol consumption, smoking and sleep apnea. This study, pioneer in Latin America, highlights the importance of integrating risk scores based on lifestyle in primary care, to identify individuals in high risk and promoting early interventions that may alter the natural history of AF. However, additional studies are required to validate its applicability in different population scenarios and to evaluate the clinical impact of its implementation.

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