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# Predictive model for atrial fibrillation in hypertensive diabetic patients

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## Abstract

**Background:** Several scores to identify patients at high risk of suffering atrial fibrillation have been developed. Their applicability in hypertensive diabetic patients, however, remains uncertain. Our aim is to develop and validate a diagnostic predictive model to calculate the risk of developing atrial fibrillation at five years in a hypertensive diabetic population.

**Methods:** The derivation cohort consisted of patients with both hypertension and diabetes attended in any of the 52 primary healthcare centres of Barcelona; the validation cohort came from the 11 primary healthcare centres of Terres de l'Ebre (Catalonia South) from January 2013 to December 2017. Multivariable Cox regression identified clinical risk factors associated with the development of atrial fibrillation. The overall performance, discrimination and calibration of the model were carried out.

**Results:** The derivation data set comprised 54 575 patients. The atrial fibrillation rate incidence was 15.3 per 1000 person/year. A 5-year predictive model included age, male gender, overweight, heart failure, valvular heart disease, peripheral vascular disease, chronic kidney disease, number of antihypertensive drugs, systolic and

diastolic blood pressure, heart rate, thromboembolism, stroke and previous history of myocardial infarction. The discrimination of the model was good (c-index = 0.692; 95% confidence interval, 0.684-0.700), and calibration was adequate. In the validation cohort, the discrimination was lower (c-index = 0.670).

**Conclusions:** The model accurately predicts future atrial fibrillation in a population with both diabetes and hypertension. Early detection allows the prevention of possible complications arising from this disease.

**KEYWORDS**

atrial fibrillation, diabetes, hypertension, incidence, prediction models

## 1 | INTRODUCTION

Worldwide, atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in adults with a current prevalence of 2%–4%.[1] It has been estimated that one in three European citizens aged over 55 years will develop this condition.[2] Patients with AF have a fivefold greater risk of stroke, a higher incidence of heart failure and increased mortality.[3] AF is commonly observed in diabetic patients, and prevalence rates are estimated to be at least double that of nondiabetic subjects.[4] Moreover, in diabetic patients with hypertension, a frequent coexisting condition, AF prevalence is up to three times higher than in AF patients with only hypertension or diabetes.[5]

Hypertension is the most common risk factor associated with AF.[3] Indeed, it has been reported that the risk for new-onset AF almost doubles, and progression to permanent AF multiplies by 1.5, when this condition is present.[6] The pathophysiological mechanisms by which hypertension leads to AF are multiple: persistently high pressures can produce ventricular hypertrophy, insufficient muscle relaxation and consequently left atrial overload, fibrosis and structural remodelling at this level. Activation of the renin-angiotensin-aldosterone system may also be one of the inducers of AF in certain hypertensive patients. Both angiotensin and aldosterone are pro-inflammatory molecules that cause fibrosis in the atrium, which is closely related to AF.[7] Individuals with hypertension and AF have a high prevalence of comorbidities, which raises the risk of all-cause mortality and thromboembolic events.[8]

With respect to diabetes mellitus, a higher risk of suffering a cardiovascular disease, and at least twice the risk of a fatal event when it is present, has been reported.[9] Diabetes is related to an increase in the size of the left atrium, regardless of hypertension or diastolic function; it also causes sympathetic and parasympathetic denervation at the same level.[10]

A reliable, easy-to-apply tool that allows early detection of AF is crucial in clinical practice, particularly in hypertensive and diabetic patients. AF may remain undiscovered for months or years and is often undiagnosed or untreated until stroke occurs. Due to the lack of AF detection in the early stages, stroke constitutes the first manifestation of unknown AF in 25% of cases.[11]

Several scores predicting the risk of developing AF have already been created, such as the CHARGE-AF Consortium,[12] the Framingham Heart Study,[13] Atherosclerosis Risk in Communities (ARIC),[14] Women's Health Study,[15] LADS[16] and HATCH score.[17] Nevertheless, none of them is specific for predicting AF in hypertensive diabetic patients who are at greater risk. Moreover, the prognostic variables necessary to predict AF, and the individual weights of these variables in the construction of the risk function, may vary slightly compared to those of the general population.

The aim of this study was to develop and validate a diagnostic predictive model to calculate the risk of developing AF in a hypertensive diabetic population.

## 2 | MATERIALS AND METHODS

We first created a prediction model with information from patient medical records to calculate the probability of AF occurrence in a hypertensive diabetic individual at 5 years. Then, we validated the developed prediction rule internally using bootstrap techniques (derivation study). Finally, we validated this rule externally with data from a comparable patient sample (validation study).

### 2.1 | Patients

Data used to create the derivation cohort were drawn from the database of patients attended in any of the 52 primary healthcare centres of the *Institut Català de la Salut* in Barcelona. Inclusion criteria were to be aged >50 years with a diagnosis of both hypertension and diabetes and without AF diagnosis at 1 January 2013. Patients with chronic inflammatory diseases, malignant neoplasm and dementia were excluded.

The cohort had a 5-year follow-up from January 2013 to December 2017.

Outcome was the first registration of an AF diagnosis, defined as a heart condition that causes an irregular and often abnormally fast heart rate (https://www.nhs.uk/conditions/atrial-fibrillation/). AF is registered in medical records using the International Diseases Classification code I48.

The validation cohort came from the 11 primary healthcare centres in Terres de l'Ebre (Catalonia South) The information was collected in the same manner as the derivation data, from January 2013 to December 2017.

## 2.2 | Prognostic factors

Medical history and demographic characteristics were used to categorize patients' prognostic variables for the predicted AF model. They included gender, age, smoking status, alcohol risk (nondrinking, nonrisk drinking and high-risk drinking, defined as a consumption of >=28 standard drink units in men and >=17 in women) and laboratory information (systolic (SBP) and diastolic blood pressure (DBP), body mass index (BMI) and heart rate). Comorbidities included hypercholesterolaemia, myocardial infarction, peripheral vascular disease, valvular heart disease, heart failure, thromboembolism, stroke, chronic renal disease and treatment related to antihypertensive drugs. Antihypertensive treatment was analysed as the number of prescribed drugs and categorized as 0-1, 2 and ≥3. BMI (kg/m2) was classified as normal weight (18.5-24.9), overweight (25-29.9), obese or severely obese (30-39.9) and morbid obese (>40).

## 2.3 | Statistical analysis

Continuous prognostic variables were described as means and standard deviation and categorical ones as percentages and frequencies. Cox proportional regression was used to establish predictors associated with AF development in univariate and multivariate analyses. Clinically meaningful variables showing a significant level in the univariate analysis ($P$-values < .1) were thereafter included in the multivariate analysis. A backward stepwise analysis was employed to identify independent potential risk predictors. A multiple imputation by chained equations was used to deal with the missing values of the prognostic variables. Forty data sets were performed, and the values combined using Rubin's rules.[18] The proportional-hazards assumption of the model was checked with scaled Schoenfeld residuals. The overall performance of the prediction model was assessed with the integrated Brier score.[19] In addition, the discriminate ability of the prediction model was assessed with Harrell's c-index.[20] We studied the calibration of the AF occurrence prediction model by plotting the predicted probability and the observed probabilities of the model in groups defined by the deciles of the predicted event probabilities.[21] We calculated the adjustment or correction of the model's performance using 500 bootstrap samples (internal validation).[22] A prognostic index (PI) for AF at 5 years was calculated for each hypertensive diabetic patient as the sum of the predictors included in the multivariate model multiplied by the log of the respective hazard ratios or by their regression coefficient ($b$). The equation was $PI = b_1 \times X_1 + b_2 \times X_2 + \ldots .+ b_k \times X_k$. To create a prognostic group, we categorized the PI into four groups at the 25th, 50th and 75th centiles, which were labelled low-, medium-low-, medium-high- and high-risk groups for AF development. Additionally, using the Cox model we calculated the predicted probability at 5 years for hypertensive diabetic patients, according to the expression $1\text{-}S_o(t)^{\exp(PI)}$, with baseline survival function at 5 years, using the Breslow estimation of the cumulative baseline hazard.[23]

The external validation of the predictive model was also evaluated in terms of both calibration and discrimination.

Analysis was performed using R software for Windows version 4.0.3 (R project for statistical computing; Vienna, Austria).

This study protocol was approved by two ethics committees, Valle Hebron Research Institute and IDIAP Jordi Gol. Data were totally anonymized to perform the analysis.

# 3 | RESULTS

The derivation data set was made up of 54 575 hypertensive diabetic patients. Follow-up time ranged from 1 to 60 months (median 60 months). AF developed in 3745 subjects, representing an incidence of 15.3 per 1000 person/year. Women represented 51.7%, and the mean age was 72.1(SD: 10.4) years. Most of the patients were nonalcohol consumers (76.8%), but active smokers (72%). Mean BMI was 30.2 kg/$m^2$ (SD: 5.04), and the mean SBP and DBP were 136 (SD: 13.1) and 75 (SD: 8.65) mm Hg, respectively. The most prevalent comorbidities at baseline were hypercholesterolaemia (57.5%), chronic renal disease (18.8%) and stroke (11.3%). In relation to antihypertensive medication, 11.9% of the patients took ≥3 antihypertensives daily. In the univariate analysis, the potential predictive variables were gender, age, smoking status, BMI, SPB, DPB, heart rate, all the cardiovascular commodities, chronic renal disease and the number of antihypertensive drugs (Table 1). The multivariate analysis identified gender, age, BMI, SBP, DBP, heart rate, myocardial infarction, peripheral artery disease, valvular heart disease, heart failure, thromboembolism, stroke, chronic kidney disease and the number of antihypertensive drugs as independent AF predictors (Table 2).

**TABLE 1** Participant characteristics and unadjusted association between each predictor and outcome

| | Total N = 54 575 | No event N = 50 830 | Event N = 3745 | Hazard ratio [95% CI] | *P* value | N |
|---|---|---|---|---|---|---|
| Gender: women (%) | 28 054 (51.4) | 26 293 (51.7) | 1761 (47.0) | 0.83 [0.78;0.89] | <.001 | 54 575 |
| Age (years) | 72.3 (10.4) | 72.1 (10.5) | 75.7 (8.49) | 1.04 [1.04;1.05] | <.001 | 54 575 |
| Age: (%) | | | | | | |
| =<64 | 13 437 (24.6) | 13 039 (25.7) | 398 (10.6) | Ref. | Ref. | 54 575 |
| 65-74 | 21 206 (38.9) | 19 468 (38.3) | 1738 (46.4) | 2.99 [2.68;3.33] | <.001 | |
| >=75 | 19 932 (36.5) | 18 323 (36.0) | 1609 (43.0) | 3.12 [2.80;3.48] | <.001 | |
| Alcohol drinking risk: (%) | | | | | | |
| Not drinking | 18 913 (76.8) | 17 429 (76.9) | 1484 (75.7) | Ref. | Ref. | 24 640 |
| Drinking not at risk | 5372 (21.8) | 4917 (21.7) | 455 (23.2) | 1.07 [0.96;1.19] | .220 | |
| High-risk drinking | 355 (1.44) | 333 (1.47) | 22 (1.12) | 0.78 [0.51;1.18] | .240 | |
| Smoking status: (%) | | | | | | |
| Nonsmoker | 1950 (28.0) | 1778 (27.5) | 172 (35.8) | Ref. | Ref. | 6957 |
| Active smoker | 5007 (72.0) | 4699 (72.5) | 308 (64.2) | 0.70 [0.58;0.84] | <.001 | |
| Clinical and analytical variables | | | | | | |
| Body mass index (kg/m$^2$) | 30.2 (5.04) | 30.1 (5.02) | 30.9 (5.27) | 1.03 [1.02;1.03] | <.001 | 27 210 |
| Body mass index (%) | | | | | <.001 | 27 210 |
| Normal | 3490 (12.8) | 3268 (13.0) | 222 (10.4) | Ref. | Ref. | |
| Overweight | 11 135 (40.9) | 10 340 (41.2) | 795 (37.2) | 1.08 [0.93;1.25] | .315 | |
| Obese | 11 383 (41.8) | 10 393 (41.5) | 990 (46.3) | 1.30 [1.12;1.50] | <.001 | |
| Morbid obese | 1202 (4.42) | 1071 (4.27) | 131 (6.13) | 1.66 [1.34;2.06] | <.001 | |
| Systolic blood pressure (mm Hg) | 136 (13.1) | 136 (13.1) | 136 (13.8) | 1.00 [1.00;1.01] | .014 | 39 027 |
| Diastolic blood pressure (mm Hg) | 75.0 (8.64) | 75.2 (8.65) | 73.3 (8.36) | 0.97 [0.96;0.97] | <.001 | 39 005 |
| Heart rate (bpm) | 75.7 (11.3) | 75.9 (11.3) | 73.5 (11.5) | 0.98 [0.98;0.98] | <.001 | 31 845 |
| Pulse pressure | 60.7 (12.5) | 60.4 (12.5) | 63.1 (13.0) | 1.02 [1.01;1.02] | <.001 | 38 905 |
| Glycated haemoglobin (%) | 7.21 (1.28) | 7.22 (1.28) | 7.20 (1.20) | 0.99 [0.96;1.02] | .681 | 33 147 |
| Comorbidity | | | | | | |
| Hypercholesterolaemia (%) | 31 388 (57.5) | 29 272 (57.6) | 2116 (56.5) | 0.94 [0.88;1.00] | .050 | 54 575 |
| Myocardial infarction (%) | 3061 (5.61) | 2736 (5.38) | 325 (8.68) | 1.75 [1.56;1.96] | <.001 | 54 575 |
| Peripheral vascular disease (%) | 3297 (6.04) | 2972 (5.85) | 325 (8.68) | 1.66 [1.48;1.86] | <.001 | 54 575 |
| Valvular heart disease (%) | 2243 (4.11) | 1926 (3.79) | 317 (8.46) | 2.43 [2.17;2.73] | <.001 | 54 575 |
| Heart failure (%) | 2836 (5.20) | 2448 (4.82) | 388 (10.4) | 2.71 [2.44;3.01] | <.001 | 54 575 |
| Thromboembolism (%) | 2162 (3.96) | 1960 (3.86) | 202 (5.39) | 1.43 [1.24;1.65] | <.001 | 54 575 |
| Stroke (%) | 6194 (11.3) | 5598 (11.0) | 596 (15.9) | 1.66 [1.52;1.81] | <.001 | 54 575 |
| Chronic renal disease (%) | 10 247 (18.8) | 9273 (18.2) | 974 (26.0) | 1.69 [1.57;1.82] | <.001 | 54 575 |
| Number of antihypertensive drugs (%) | | | | | <.001 | 54 575 |
| 0-1 | 32 961 (60.4) | 31 232 (61.4) | 1729 (46.2) | Ref. | Ref. | |
| 2 | 15 125 (27.7) | 13 883 (27.3) | 1242 (33.2) | 1.60 [1.49;1.72] | <.001 | |
| >=3 | 6489 (11.9) | 5715 (11.2) | 774 (20.7) | 2.47 [2.27;2.68] | <.001 | |
| Diabetes duration (years) | 7.95 (6.15) | 7.91 (6.15) | 8.43 (6.23) | 1.02 [1.01;1.02] | <.001 | 54 534 |
| Hypertension duration (years) | 8.95 (6.14) | 8.88 (6.10) | 9.84 (6.50) | 1.02 [1.02;1.03] | <.001 | 54 521 |

*Note:* Values are given as mean (standard deviation) or frequency (percentage).

Our AF predictive model demonstrated a good discrimination ability with an apparent c-index at 5 years of 0.692 (95% CI, 0.684-0.700) and an optimism-corrected c-index of 0.69. In addition, the overall performance using the integrated Bier score showed a score (0.03) below 0.25. In terms of agreement between the predicted and observed probabilities

**TABLE 2** Multivariate Cox model, including the baseline survival at 5 years and the expression to calculate the prognostic index of AF

| Variables | Regression coefficient | *P* value | Hazard ratio [95% CI] |
|---|---|---|---|
| Gender: women | −0.452 | <.001 | 0.64 [0.59; 0.69] |
| Age (years) | 0.044 | <.001 | 1.05 [1.04; 1.05] |
| Body mass index | | | |
| Normal | 0 | - | Ref. |
| Overweight | 0.304 | .008 | 1.35 [1.17; 1.57] |
| Obese | 0.636 | <.001 | 1.89 [1.59; 2.24] |
| Morbid obesity | 1.039 | <.001 | 2.83 [2.13; 3.75] |
| Systolic blood pressure (mmHg) | 0.001 | .299 | 1.00 [1.00;1.01] |
| Diastolic blood pressure (mmHg) | -0.007 | <.001 | 0.99[0.98;0.99] |
| Heart rate (bpm) | -0.009 | <.001 | 0.99 [0.98; 0.99] |
| Myocardial infarction | 0.156 | .010 | 1.17 [1.04; 1.32] |
| Peripheral vascular disease | 0.214 | <.001 | 1.24 [1.10; 1.39] |
| Valvular heart disease | 0.559 | <.001 | 1.75 [1.55; 1.97] |
| Heart failure | 0.375 | <.001 | 1.46 [1.30; 1.63] |
| Thromboembolism | 0.220 | .003 | 1.25 [1.08; 1.44] |
| Stroke | 0.248 | <.001 | 1.28 [1.17; 1.40] |
| Chronic kidney disease | 0.116 | .003 | 1.12 [1.04; 1.50] |
| Number of antihypertensive drugs | | | |
| 0-1 | 0 | - | Ref. |
| 2 | 0.332 | <.001 | 1.39 [1.29; 1.50] |
| >=3 | 0.574 | <.001 | 1.77 [1.62; 1.95] |

*Note:* $S_0(5)$= 0.995 (5 years of baseline survival). β-values are expressed per 1 unit increase for continuous variables and for the condition present in categorical variables. The predictive probability to develop a AF was determined by $1\text{-}S_0(5)^{\exp(PI)}$, and PI = −0.452xWoman+ 0.044xAge +0.304xOverweight+ 0.636xObese+1.039xMorbidiyObses+0.001xSBP-0.007xDBP-0.009xHeart_Rate+0.156xMyocardial Infarction+0.214xPeripheral vascular disease+0.559xValvular heart disease+0.375xHeart Failure +0.220xThromboembolism+0.248xStroke+0.116xChronic kidney disease+0.332x(2antihypertensive) +0.574x(>=3 antihypertensive).

of the risk of developing an AF, both smoothness lines (the apparent and the optimism correction) lie around a 45 line of the plot with a slope of 1 (an optimism-corrected slope of 0.9897; Figure 1).

The risk groups based on the 25th, 50th and 75th centiles of the PI were defined as low with PI lower than 2.267, medium-low with PI between 2.267 and 2.702, medium-high with PI between 2.702 and 3.161, and the highest with PI greater than 3.161. The incidence of these risk groups was 4.95, 10.62, 20.70 and 36.60 per 1000 person/year, respectively. The cumulative incidence for PI risk groups is presented in Figure 2. It can be observed that the four curves

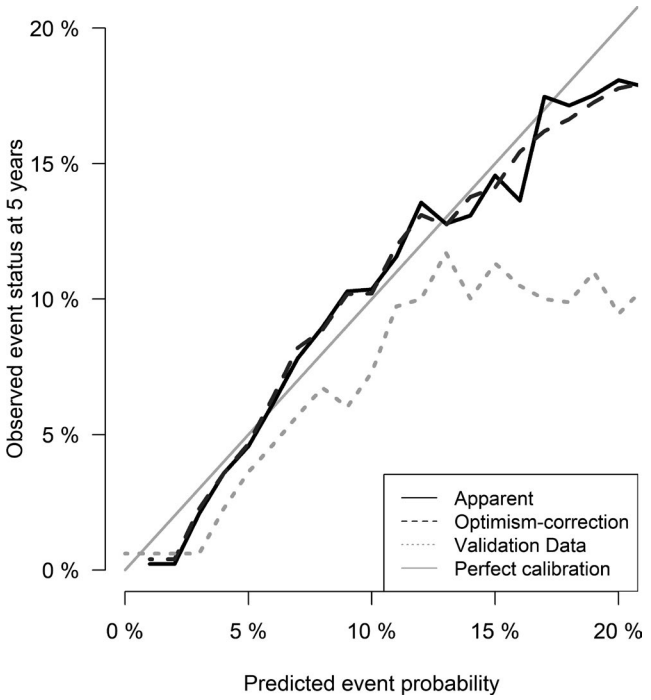


**FIGURE 1** Calibration of predictions using bootstrap validation; back line shows apparent calibration in the derivation cohort, grey long dash shows optimism-corrected calibration in the derivation cohort, grey dotted line shows calibration in the validation cohort, and light grey line shows the x = y line

are quite well separated, indicating good discrimination of the patients (log-rank = 870.4, $P < .001$). In addition, considering the reference group as the low risk, the hazard ratio for the medium-low-risk group was 2.15 (95% CI 1.76-2.62), 4.20 (95% CI 3.50-5.05) for the medium-high-risk group and 7.50 (95% CI 6.27-8.94) for the high-risk group .

The web-based risk calculator is available at https://rabellana.shinyapps.io/RiskCalculatorAF/

## 3.1 | External validation study

For the external validation, the data set from Terres de l'Ebre was made up of 7145 patients. Of these, 3080 had data available to calculate the PI. Patients had a median follow-up of 60 months. The baseline characteristics of these subjects differed significantly from those in the derivation cohort in that they were older and presented a lower prevalence of comorbidities (Table 3). Overall, 178 (5.8%) of the 3080 developed AF during the 5-year follow-up, resulting in an incidence of 12.25 per 1000 person/year. Thus, 588 (19.0%) were classified as low risk, 684 (22.2%) as medium-low risk, 789 (25.6%) as medium-high risk and 1019 (33.1%) as high risk. The incidence for these risk groups was 2.41, 8.19, 12.88 and 20.85 per 1000 person/year, respectively, with a smaller c-index value (0.67). Hazard ratios among the risk groups were 3.40 (95% CI 1.48-7.82) for the medium-low, 5.36 (95% CI 2.42-11.84) for the medium-high and 8.71 (95% CI 4.04-18.76) for the high risk. The hazard

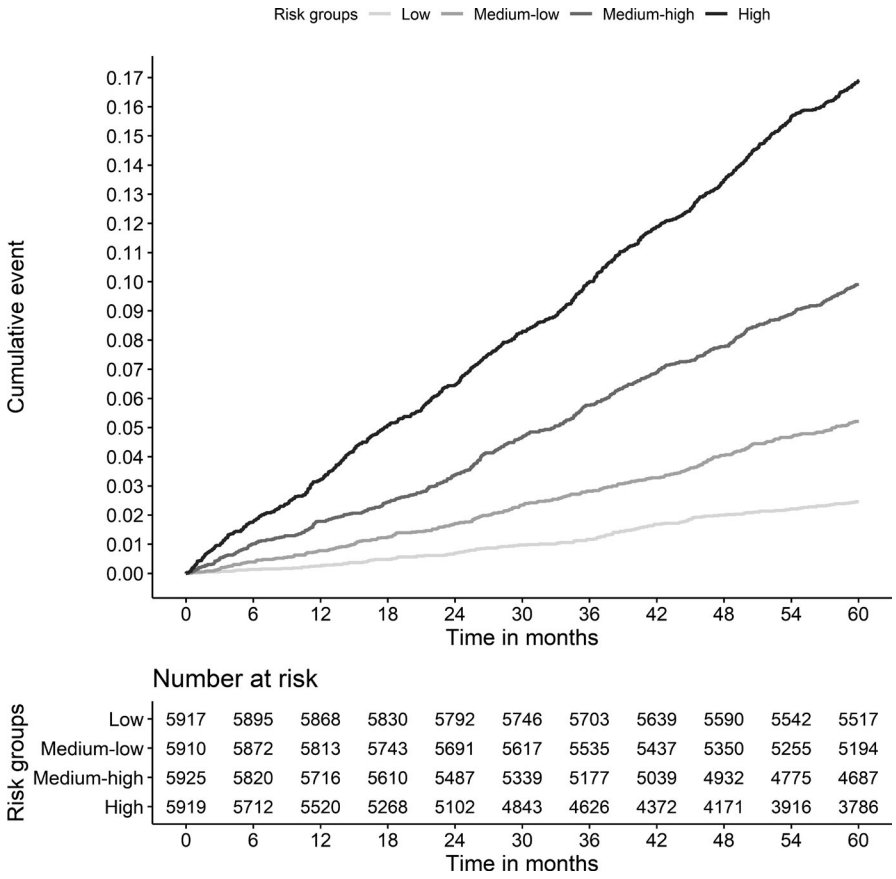


**FIGURE 2** Cumulative incidence (Kaplan-Meier estimator) of developing an atrial fibrillation in four risk groups (lower risk with PI lower than 2.267, medium-low with PI between 2.267 and 2.702, medium-high with PI between 2.702 and 3.161, and the highest with PI greater than 3.161) in the derivation cohort

ratios obtained in the derivation data set were well maintained in the validation one. The cumulative incidence for PI risk groups in the validation cohort is depicted in Figure 3. In terms of calibration, however, the long grey dash line shows that the predicted probabilities of the AF development model were slightly greater than the observed probabilities in the external set.

## 4 | DISCUSION

In hypertensive diabetic patients, the identified predictive variables of AF risk were age, male gender, overweight, heart failure, valvular heart disease, peripheral vascular disease, chronic kidney disease, number of antihypertensive drugs, SBP, DBP, heart rate and thromboembolism. From a clinical perspective, our risk model will help clinicians to evaluate the risk of AF developing in a high-risk population.

Predictive models for AF carried out in a general population, such as CHARGE-AF Consortium[12] and Mayo Clinic,[24] include several prognostic variables. Nevertheless, only a few of them are common in both scores, for instance heart failure, age, coronary heart disease, diabetes mellitus and hypertension, demonstrating the consistency and importance of these conditions with respect to AF. When we tested the CHARGE predictive model in our population, we found a reduction in its predictive capacity, the c-index decreasing from 0.76 to 0.66, whilst the Mayo Clinic model showed a c-index of 0.66.

To the best of our knowledge, no models specifically predicting the risk of AF in patients simultaneously presenting hypertension and diabetes have been reported. Yang et al developed a predictive model for diabetic patients[25] and found that age, gender, race, history of heart failure, DBP, BMI, triglycerides, glycated haemoglobin (HbA1c), diabetes duration, hypertensive medication and creatinine presented a concordance similar to our model. Regarding hypertension, Orozco-Beltran et al worked on a model to predict AF risk in a population with this condition. They included age, male gender, obesity and heart failure as independent predictors and reported a slightly lower concordance.[26]

In our cohort, the number of antihypertensive drugs needed to control blood pressure was related to a higher AF risk. It has been reported that adequate management of hypertension may prevent AF by reducing atrial stretch and suppressing electrical and structural cardiac remodelling.[27,28]

In line with our findings, an increased risk of AF related to obesity, due to its deleterious effect on hypertension and diabetes, has been published.[29,30]

Cardiovascular diseases and risk factors (heart failure, valvular heart disease, myocardial infarction, peripheral vascular disease and chronic kidney disease) presented an association with AF in our study, as expected according to published evidence.[31] In addition, higher mortality rates have been found in patients with heart failure.[32]

**TABLE 3** Comparison of participant characteristics in derivation and validation cohorts

| | Derivation cohort (N = 54 575) | Validation cohort (N = 7145) | *P* Value |
|---|---|---|---|
| Gender: women (%) | 28 054 (51.4%) | 3637 (50.9%) | .426 |
| Age (years) | 72.3 (10.4) | 77.1 (11.9) | <.001 |
| Body mass index (%) | | | |
| Normal | 3490 (12.8%) | 284 (8.49%) | <.001 |
| Overweight | 11 135 (40.9%) | 1238 (37.0%) | |
| Obese | 11 383 (41.8%) | 1611 (48.2%) | |
| Morbidity obese | 1202 (4.42%) | 212 (6.34%) | |
| Systolic blood pressure (mmHg) | 75.0 (8.64) | 76.3 (8.64) | <.001 |
| Diastolic blood pressure (mmHg) | 75.0 (8.64) | 76.3 (8.64) | <.001 |
| Heart rate (bpm) | 75.7 (11.3) | 75.3 (11.3) | .012 |
| Hypercholesterolaemia (%) | 31 388 (57.5%) | 2022 (28.3%) | <.001 |
| Myocardial infarction (%) | 3061 (5.61%) | 145 (2.03%) | <.001 |
| Peripheral vascular disease (%) | 3297 (6.04%) | 288 (4.03%) | <.001 |
| Valvular heart disease (%) | 2243 (4.11%) | 218 (3.05%) | <.001 |
| Heart failure (%) | 2836 (5.20%) | 163 (2.28%) | <.001 |
| Thromboembolism (%) | 2162 (3.96%) | 251 (3.51%) | .070 |
| Stroke (%) | 6194 (11.3%) | 14 (0.20%) | <.001 |
| Chronic renal disease (%) | 10 247 (18.8%) | 221 (3.09%) | <.001 |
| Number of antihypertensive drugs (%) | | | |
| 0-1 | 32 961 (60.4%) | 4308 (60.3%) | .663 |
| 2 | 15 125 (27.7%) | 2009 (28.1%) | |
| >=3 | 6489 (11.9%) | 829 (11.6%) | |

*Note:* Values are given as mean (standard deviation) or frequency (percentage).

Higher SBP was related to greater AF incidence which also concurs with other studies.[12,14] Tremblay et al observed that SBP >140 mmHg was associated with an increased risk of recurrent AF in subjects who have left ventricular systolic dysfunction (LVEF <40%). We have no available data concerning ejection fraction in our cohort to precisely classify such results.[7] Muria-Subirats et al also reported an inverse relationship between heart rate and DBP with AF in diabetic and hypertensive patients, that is to say, patients with a lower heart rate and DBP were more likely to develop AF.[33]

Several scores had been created for measuring AF risk across a broad spectrum of the general population. Nevertheless, our model specifically provides an accurate classification for hypertensive diabetic patients, a group at an elevated risk, by facilitating on-time diagnosis. Among the predictive variables, only blood pressure and body weight could be prevented. However, the early detection of high AF risk permits a close follow-up and better management to prevent the occurrence of this disease, and eventually serves to prevent the terrible consequences of arrhythmia, mainly stroke.

## 5 | LIMITATIONS AND STRENGTHS

Our predictive model has been calculated in an elderly population; hence, its use in younger populations must be carefully considered.

Our study data come from a large administrative database which enables a good external validity of the predictive model.

Although the populations of the derivation and validation models were geographically different, this allowed the model to be implemented in different settings.

## 6 | WHAT'S NEW

- A predictive tool for AF focused on hypertensive diabetic individuals with pre-existing risk for this arrhythmia.
- Accurate classification of patients at the highest risk of AF provides the opportunity to prevent future complications.
- Thromboembolism and stroke should be considered not only as consequences of AF but also as predictive variables for this arrhythmia

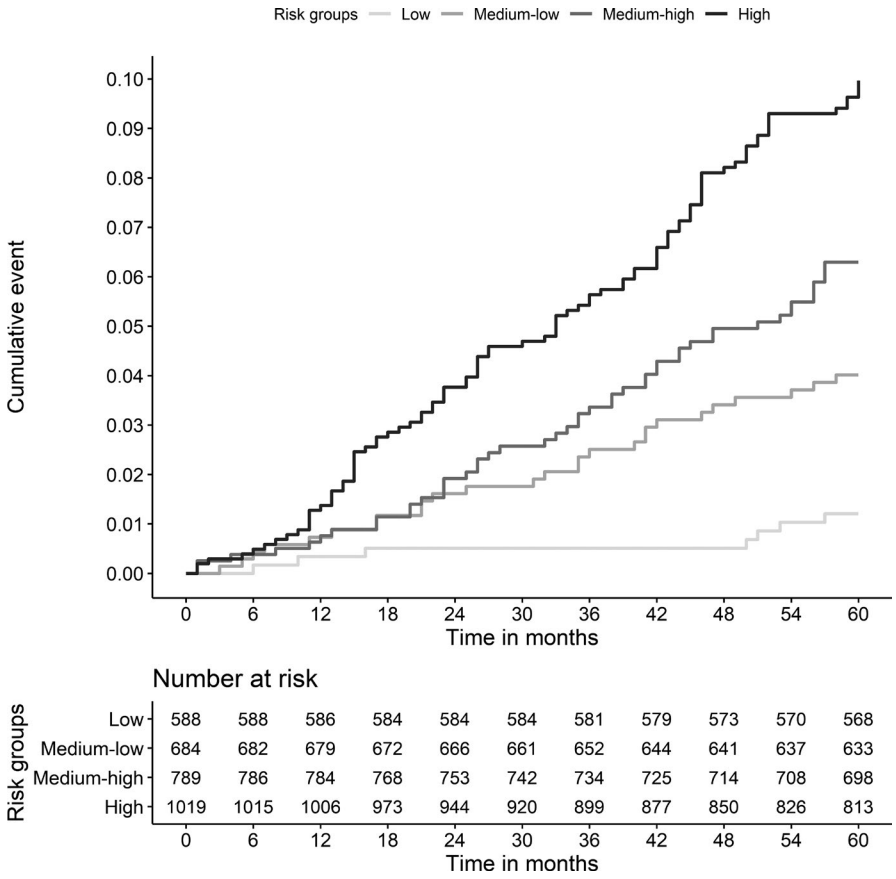


**FIGURE 3** Cumulative incidence (Kaplan-Meier estimator) of developing an atrial fibrillation in four risk groups (low risk with PI lower than 2.267, medium-low with PI between 2.267 and 2.702, medium-high with PI between 2.702 and 3.161, and the highest with PI greater than 3.161) in the validation cohort

## CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interests, and there has been no financial support for this work.

## AUTHOR CONTRIBUTIONS

Guarantors of integrity of entire study, HHS, SHP; study concepts, SSH, SHP, KHC; study design, SSH, HHS, YHP; literature research, SSH; data acquisition, SSH, JHB, SLJ; data analysis/interpretation, SSH, JHB, SHP; statistical analysis, HHS, JHB; manuscript preparation, SSH, HHS; manuscript definition of intellectual content, HHS, SHP; manuscript editing, HHS, SSH; manuscript revision/review and final version approval, all authors Guarantors of integrity of entire study: Rosa Abellana and Miguel Angel Muñoz. Study concepts and design: Rosa Abellana, Felipe Gonzalez-Loyola, Jose- Maria Verdu-Rotellar, Alejandro Bustamante, Elena Palà, Josep Lluis Clua-Espuny, Joan Montaner, Alonso Pedrote, Domingo Ribas Segui and Miguel Angel Muñoz. Data acquisition: Jose Luis del Val-Garcia. Statistical Analysis: Rosa Abellana. Interpretation of the results: All authors. Manuscript preparation: Rosa Abellana, Miguel Angel Muñoz and Felipe Gonzalez-Loyola. Manuscript revision/review and final version approval: All authors.

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