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Demographic Refinement and Atrial Fibrillation Type in Stroke Risk Stratification beyond CHA_2DS_2 VASc

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Keywords
Ischaemic stroke · Transient ischaemic attack · Atrial fibrillation · Risk prediction

Abstract

Introduction: The CHA_2DS_2 VASc score is widely used for stroke risk stratification in atrial fibrillation (AF). Efforts to improve prediction using demographic refinements have uncertain incremental value, particularly in multi-ethnic populations. We evaluated whether demographic modification or AF type provides additional discriminatory value. ***Methods:*** We conducted a retrospective nested case-control study of patients with AF diagnosed prior to the fifth Auckland Regional Community Stroke Study (September 2020–August 2021). Cases with ischaemic stroke or transient ischaemic attack were identified from this population-based registry with central adjudication. Controls were randomly selected from the National Minimum Dataset, stratified by ethnicity. Predictors included CHA_2DS_2 VASc components, demographic refinements (alternative age transformations, ethnicity, and exclusion of sex), and AF type. The primary baseline model was a multivariable logistic regression model using standard CHA_2DS_2 VASc predictors as covariates. The traditional point-based CHA_2DS_2 VASc score was evaluated separately for comparison. Discrimination was assessed using the area under the receiver operating characteristic curve (AUC). ***Results:*** The study included 1,908 patients (300 cases). A logistic regression model using standard CHA_2DS_2 VASc predictors demonstrated moderate discrimination {AUC 0.68 (95% confidence interval [CI]: 0.65–0.71)}. The traditional point-based CHA_2DS_2 VASc score showed lower discrimination (AUC 0.63 [95% CI: 0.60–0.66]; ΔAUC +0.05; p = 0.0003). Demographic refinements did not improve discrimination (ΔAUC ≤ 0.01). Addition of AF type

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modestly increased discrimination (AUC 0.71; ΔAUC +0.03; $p = 0.015$), with greater improvement in non-anticoagulated patients (ΔAUC +0.05). ***Conclusion:*** Demographic refinements, including ethnicity, provide limited incremental value beyond CHA_2DS_2 VASc, whereas AF type offers a modest discriminatory signal. This finding is hypothesis-generating and requires external validation before clinical implementation is considered.

Introduction

Stroke risk stratification in atrial fibrillation (AF) is central to guiding anticoagulation use to prevent ischaemic stroke (IS). The CHA_2DS_2 VASc score remains the most widely used clinical tool, but its predictive performance is modest, with reported discrimination typically ranging from 0.55 to 0.70 in external validation studies [1]. It includes clinical and demographic factors of cardiac failure, hypertension, age ≥75 years [doubled], previous IS/transient ischaemic attack (TIA) [doubled], vascular disease, and female sex.

Efforts to improve risk prediction have largely focused on demographic refinement, including alternative modelling of age, incorporation of ethnicity, and removal of the female sex component [2, 3]. However, the incremental value of these approaches remains uncertain, particularly in contemporary multi-ethnic populations. Ethnicity is an important social determinant of health in New Zealand, with Māori and Pacific people developing AF and experiencing IS over one decade earlier than Europeans [1, 4]. Auckland's population (1.9M) is ethnically diverse, comprising approximately 12% Māori, 14% Pacific peoples, 37% Asian (East and South), and 38% European or other ethnicities [5]. We evaluated whether demographic refinement or AF type improves stroke risk prediction beyond CHA_2DS_2 VASc.

Methods

We conducted a retrospective nested case-control study of patients with AF diagnosed prior to the fifth Auckland Regional Stroke Study (ARCOS V, 1 September 2020–31 August 2021). In short, ARCOS is a prospective population-based registry capturing stroke and TIA events across Auckland using multiple overlapping ascertainment sources, with central diagnostic adjudication [6]. Cases were obtained from ARCOS V. Controls were randomly selected from the New Zealand National Minimum Dataset using ICD-10 AF (I48) codes, and did not experience IS/TIA during ARCOS V. Controls were stratified by ethnicity to ensure adequate representation of major ethnic groups; no weighting or conditional methods were applied, as analyses focused on comparing relative model discrimination within the sampled dataset rather than estimation of population incidence or calibration.

All AF diagnoses and comorbidities were confirmed through structured clinical record review. Patients with transient cardiac surgery-associated AF, moderate-to-severe mitral stenosis/mechanical heart valves, or AF diagnosed at the time of the outcome event were excluded. Cases and controls were drawn from patients receiving secondary care across the three major Auckland hospital networks. The prediction horizon was an incident IS/TIA occurring during the ARCOS V observation period (1 September 2020 to 31 August 2021), using predictor information available up to 31 August 2020.

Predictor variables were defined according to CHA_2DS_2 VASc components, with additional evaluation of demographic refinements (including alternative age transformations, ethnicity, and exclusion of female sex) and AF type (paroxysmal vs. persistent/permanent). AF pattern was determined using a hierarchical approach: (1) explicit clinician documentation where available; (2) otherwise, classification based on serial electrocardiograms, echocardiography reports, and clinical notes demonstrating either paroxysmal episodes with reversion to sinus rhythm or continuous AF without reversion. AF pattern could be determined for all patients using hospital records, and there were no cases with indeterminate classification.

Ethnicity was self-identified and classified using New Zealand's prioritised ethnicity system, whereby individuals reporting multiple ethnicities are assigned to a single category in a predefined order (Māori, Pacific peoples, European, and Other) [7]. Ethnicity, comorbidities, and AF pattern could be determined for all patients, with no missing data.

Anticoagulation status was included as a covariate in all primary discrimination models because treatment substantially modifies observed stroke risk in contemporary AF populations. Additional analyses were stratified by anticoagulation status to assess whether the discriminatory value of AF type differed according to treatment exposure. Anticoagulant exposure was assessed during ARCOS V over a median 156-day period (IQR 138–204), including the period leading up to the index IS/TIA event for cases.

Table 1. Baseline characteristics of cases and controls

Variables	Overall	Cases	Controls
	N = 1,908	*N* = 300	*N* = 1,608
Median age (IQR) years	70 (61–79)	77 (67–84)	69 (60–77)
Female, *n* (%)	892 (46.8)	145 (48.3)	747 (46.5)
Ethnicity, *n* (%)			
European	747 (39.2)	128 (42.7)	619 (38.5)
Māori	403 (21.2)	61 (20.3)	342 (21.3)
Pacific peoples	547 (28.7)	69 (23.0)	478 (29.3)
Others	211 (11.1)	42 (14.0)	169 (10.5)
Comorbidities, *n* (%)			
Left ventricular failure	344 (18.0)	48 (16.0)	296 (18.4)
Hypertension	1,215 (63.7)	207 (69.0)	1,008 (62.7)
Diabetes	556 (29.1)	92 (30.7)	464 (28.9)
Prior IS/TIA	338 (17.7)	87 (29.0)	251 (15.6)
Vascular disease	565 (29.6)	98 (32.7)	467 (29.0)
Median CHA_2DS_2 VASc score (IQR)	3 (2–4)	4 (3–5)	3 (2–4)
Persistent/permanent AF, *n* (%)	1,039 (55.5)	218 (72.7)	821 (51.1)
Aspirin, *n* (%)	246 (12.9)	51 (17.0)	195 (12.1)
Anticoagulation, *n* (%)	1,315 (68.9)	179 (59.7)	1,136 (70.7)
Warfarin	214 (16.3)	30 (16.8)	184 (16.2)
Rivaroxaban	265 (20.2)	35 (19.6)	230 (20.3)
Dabigatran	836 (63.6)	114 (63.7)	722 (63.6)

Controls were sampled using ethnicity-stratified random selection. IQR, interquartile range; IS, ischaemic stroke; TIA, transient ischaemic attack; AF, atrial fibrillation.

For the discrimination analyses, the index date was 31 August 2020. Predictor variables were defined using information available on or before this date, with the exception of anticoagulant exposure, which was assessed during the ARCOS V observation period as described above. Multivariable logistic regression models were used to compare discrimination between CHA_2DS_2 VASc predictors and model refinements. The primary baseline model consisted of the standard CHA_2DS_2 VASc predictors modelled using regression coefficients. This was distinguished from the traditional point-based CHA_2DS_2 VASc score, which was evaluated separately for comparison. Discrimination was assessed using the area under the receiver operating characteristic curve (AUC) with 95% confidence intervals (CIs), and internal validation was performed using bootstrap resampling (1,000 repetitions). Differences in AUC were assessed using the DeLong test. Measures of clinical utility such as net reclassification improvement and decision curve analysis were not performed, as the nested case-control design precludes valid estimation of absolute risk and calibration. The present analysis, therefore, focuses on discrimination and relative model performance.

Analyses were performed using Stata version 17BE (StataCorp, College Station, TX) and reported in accordance with prediction modelling guidelines [8]. The study method has been published previously [3].

Results

The study included 1,908 patients with AF, including 300 with incident IS/TIA during the ARCOS V study period. Baseline characteristics are demonstrated in Table 1.

The primary baseline model demonstrated moderate discrimination (AUC 0.68, 95% CI: 0.65–0.71). The traditional point-based CHA_2DS_2 VASc score showed lower discrimination (AUC 0.63, 95% CI: 0.60–0.66; ΔAUC +0.05; $p = 0.0003$).

When modelling regression coefficients, demographic refinements, including alternative age transformations, ethnicity, and exclusion of female sex, did not improve discrimination (ΔAUC ≤ 0.01; Table 2). In contrast,

Table 2. Discrimination of CHA_2DS_2 VASc predictor structures and model refinements in a multi-ethnic AF cohort

Model	Patients, *n*	AUC (95% CI)	ΔAUC vs. baseline	*p* value
CHA_2DS_2 VASc (regression coefficients)	1,908	0.68 (0.65–0.71)	Ref	–
CHA_2DS_2 VASc (point based)	1,908	0.63 (0.60–0.66)	−0.05	0.0003
Age remodelled[a]	1,908	0.68	≤0.01	NS
Excluding female sex	1,908	0.68 (0.65–0.71)	<0.01	0.65
+ Prioritised ethnicity	1,908	0.68 (0.65–0.71)	<0.01	0.33
+ AF type	1,908	0.71 (0.68–0.74)	+0.03	0.015
Non-anticoagulated (baseline)	583	0.78 (0.73–0.82)	Ref	
Non-anticoagulated + AF type	583	0.83 (0.79–0.87)	+0.05	0.0008
Anticoagulated (baseline)	1,315	0.64 (0.59–0.68)	Ref	
Anticoagulated + AF type	1,315	0.66 (0.61–0.70)	+0.02	0.18

[a]Age was modelled as a continuous variable, using alternative categorical cut-offs, and with restricted cubic splines based on the observed age distribution (median and interquartile range).

incorporation of AF type increased discrimination (AUC 0.71 [95% CI: 0.68–0.74]; ΔAUC +0.03; $p = 0.015$). When stratified by anticoagulation status, the incremental value of AF type was greater in non-anticoagulated patients (ΔAUC +0.05; $p = 0.0008$) and attenuated in anticoagulated patients (ΔAUC +0.02; $p = 0.18$). Bootstrap-corrected estimates were similar, indicating minimal optimism.

Discussion

In this multi-ethnic, clinically validated AF cohort, a regression model using CHA_2DS_2 VASc predictors demonstrated modest discrimination, consistent with prior international studies [1]. This supports the continued applicability of the score, with little evidence of major temporal drift in performance. The traditional point-based CHA_2DS_2 VASc score demonstrated lower discrimination than a regression model using the same predictors, reflecting the information loss from fixed integer weighting. Subsequent model comparisons were performed against the regression-based baseline model as this allows a more direct assessment of the incremental value of additional predictors or refinements.

Our findings suggest that further demographic refinement is unlikely to meaningfully improve stroke risk prediction using CHA_2DS_2 VASc. Despite known differences in age at AF onset and stroke risk across ethnic groups, incorporation of ethnicity did not enhance predictive performance. This may indicate that observed disparities reflect differences in healthcare access, comorbidity burden, or treatment pathways rather than baseline clinical risk factors alone. However, this finding should be interpreted cautiously, as the use of prioritised ethnicity categories and broad groupings may reduce granularity and obscure heterogeneity within populations, potentially attenuating true prognostic associations.

Similarly, exclusion of the female sex component did not improve discrimination, consistent with emerging evidence that female sex may function more as a risk modifier than an independent risk factor in AF-related stroke. This finding supports recent moves toward simplified scores such as CHA_2DS_2 VA (exclusion of female sex), and further suggests that modification of existing demographic components is unlikely to yield meaningful gains in predictive performance [9].

In contrast, AF type provided consistent incremental discrimination beyond established predictors. Persistent or permanent AF may reflect greater cumulative arrhythmia burden and atrial remodelling, including atrial fibrosis, impaired contractility, and blood stasis, which promote thrombus formation and are not captured by traditional risk scores. The incremental discriminatory value of AF type was greater in non-anticoagulated patients and attenuated in those receiving anticoagulation, suggesting that AF phenotype may be more informative in untreated populations. This pattern likely reflects the modifying effect of anticoagulation on stroke risk, although treatment selection effects cannot be excluded.

Although the observed improvements in discrimination are modest and not practice-changing, they suggest that disease phenotype may represent a more

informative direction for future risk prediction models than continued modification of demographic factors.

Strengths of this study include clinically validated comorbidity and AF diagnosis, centrally adjudicated outcomes, and evaluation within a multi-ethnic population. Limitations include the case-control design, which precludes assessment of absolute risk, calibration or decision-curve-based clinical utility, and limits interpretation to discrimination. AF type was determined using clinician documentation, serial electrocardiograms and clinical records; however, given the episodic nature of AF and reliance on available recordings, some degree of misclassification is possible; this would be expected to bias results toward the null. External validation and evaluation of clinical applicability are required.

Conclusion

CHA_2DS_2 VASc demonstrated modest discrimination in this multi-ethnic cohort, with minimal gain from demographic refinement. AF type provided a modest, treatment-dependent signal, stronger in non-anticoagulated patients and attenuated with anticoagulation. These findings are hypothesis-generating and require external validation before any clinical implementation is considered.

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Statement of Ethics

This study has been approved by the Health and Disability Ethics Committee (HDEC) (ref: 2023 AM 9094) and the Auckland University of Technology Ethics Committee (24/4). This study was performed in accordance with the Declaration of Helsinki. Ethical approval was granted by the Auckland University of Technology Ethics Committee (reference 24/4). The requirement for written informed consent was waived by the Auckland University of Technology Ethics Committee because this was a low-risk observational study using routinely collected clinical data.

Conflict of Interest Statement

K.M.M. received a Health Research Council of New Zealand grant as part of his doctoral studies supporting this research. H.W. has received institutional grant support from Sanofi-Aventis, DalCor Pharma UK Inc, CSL Behring, National Health Institutes, Sanofi Aventis Australia Pty Ltd, Janssen Research and Development LLC and Merck Sharp & Dohme (New Zealand) Ltd. H.W. has also received travel and accommodation paid for attendance at Investigator meetings (2025) by Merck Sharp & Dohme (New Zealand) Ltd. The remaining authors have no conflicts of interest to declare.

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Author Contributions

K.M.M. designed the study and drafted the manuscript. V.F., H.W., I.S.Z., A.R., D.B., S.B.-C., and R.V.K. reviewed and contributed to the manuscript. R.V.K. assisted with obtaining approvals and funding for this study.

Data Availability Statement

The data that support the findings of this study are not publicly available due to patient privacy and institutional data governance restrictions. Anonymised data may be made available from the corresponding author on reasonable request and subject to institutional and ethical approval.

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