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Clinical Predictors of Risk for Atrial Fibrillation: Implications for Diagnosis and Monitoring

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Abstract

Objective: To create a risk score using clinical factors to determine whom to screen and monitor for atrial fibrillation (AF).

Patients and Methods: The AF risk score was developed based on the summed odds ratios (ORs) for AF development of 7 accepted clinical risk factors. The AF risk score is intended to assess the risk of AF similar to how the CHA_2DS_2-VASc score assesses stroke risk. Seven validated risk factors for AF were used to develop the AF risk score: age, coronary artery disease, diabetes mellitus, sex, heart failure, hypertension, and valvular disease. The AF risk score was tested within a random population sample of the Intermountain Healthcare outpatient database. Outcomes were stratified by AF risk score for OR and Kaplan-Meier analysis.

Results: A total of 100,000 patient records with an index follow-up from January 1, 2002, through December 31, 2007, were selected and followed up for the development of AF through the time of this analysis, May 13, 2013, through September 6, 2013. Mean ± SD follow-up time was 3106±819 days. The ORs of subsequent AF diagnosis of patients with AF risk scores of 1, 2, 3, 4, and 5 or higher were 3.05, 12.9, 22.8, 34.0, and 48.0, respectively. The area under the curve statistic for the AF risk score was 0.812 (95% CI, 0.805-0.820).

Conclusion: We developed a simple AF risk score made up of common clinical factors that may be useful to possibly select patients for long-term monitoring for AF detection.

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Atrial fibrillation (AF) affects 2.3 million Americans, is associated with an increased risk of stroke, and often occurs with other comorbidities, such as congestive heart failure.[1,2] Although anticoagulation can reduce the risk of stroke, anticoagulation can only be initiated if the diagnosis of AF is made. Because AF is often asymptomatic, it is frequently undiagnosed, and patients therefore do not undergo anticoagulation. As a consequence, these patients may be exposed to a higher risk of stroke.[3,4] This potential adverse risk is highlighted in a study that found that subclinical AF accounted for approximately 23% of cryptogenic strokes.[5] In addition, addressing AF may also positively affect other associated comorbidities.

Atrial fibrillation, especially if paroxysmal and asymptomatic, may be missed during clinical evaluations, electrocardiography, and periodic ambulatory telemetry monitoring. Screening for AF after an ischemic stroke has the anticipated benefit of identifying 4.4 new cases of AF for every 100 patients monitored.[6] With long-term continuous monitoring, as is available with implantable devices, the diagnostic yield of previously undetected AF after a stroke increases significantly.[7] Expansion of long-term monitoring to detect AF before a stroke occurs in large populations is not likely to be cost-effective or time effective, unless high-risk features for AF genesis can be determined to improve selection criteria. In addition, data from the Asymptomatic Atrial Fibrillation and Stroke Evaluation in Pacemaker Patients and the Atrial Fibrillation Reduction Atrial Pacing Trial (ASSERT) suggest that strokes often occur independently of AF episodes, and as such remote monitoring as a means to detect AF early and reduce events by starting anticoagulation may be insufficient.[8] As such, we sought to create a simple, readily accessible AF risk score according to general clinical markers to determine which patients are at highest risk of AF and should be considered for long-term

monitoring to improve early diagnosis and initiate anticoagulation strategies.

METHODS

Risk Score Basis

Initial analysis was performed on the basis of literature cited in the review by Kirchhof et al.[9] Kirchhof et al summarized data from a variety of previously published studies in regard to risk factors for AF that they further classified as validated. The validated risk factors for AF defined by Kirchhof et al included age, coronary artery disease, diabetes mellitus, sex, heart failure, hypertension, and valvular disease. To establish their validated AF risk factors, Kirchhof et al cited a total of 17 publications as sources, of which 16 were included in their risk score development meta-analysis (1 publication was excluded because all patients had AF and, therefore, could not contribute to attempts to build discriminatory models). Data from each of the 16 source documents were extracted to derive validated risk factors for AF.

Because some of these source documents presented results from a series of statistical models adjusted for different factors, we selected the simplest model presented to eliminate problems of interpretation by combining models from different covariate adjustments and to produce meta-analytic estimates closest to the aggregate unadjusted result. Odds ratios (ORs) were used if multiple metrics were presented or raw summary statistics were available. When necessary, relative risks and hazard ratios were presumed to approximate the OR to facilitate modeling. To allow for heterogeneity among studies, a random-effects meta-analysis was performed by analyzing the log ORs via restricted maximum likelihood estimation. A separate model was fit for each risk factor, with potentially different studies being included in each model, depending on the risk factor data available in the source publication.

When multiple cohorts were presented in an article, each cohort was considered as its own independent study and not combined within a publication. When not previously defined by the source article, we defined hypertension as systolic blood pressure greater than 160 mm Hg. Odds of AF according to age were calculated for 3 age strata: younger than 65, 65 through 75, and older than 75 years.

Risk Score Development

A risk score for the development of AF was created with the point estimates for the OR of each factor from the random-effects meta-analysis. Risk score points were assigned to each of the 7 risk factors with downward rounding of their respective meta-analytic ORs. The presence of each risk factor provides a contribution to the total risk score.

The meta-analysis of the 16 studies used to develop the AF risk score is summarized in Table 1. The ORs ranged from 1.5 for male sex to 3.6 for heart failure. For each risk factor, there was significant evidence of heterogeneity (all $P<.02$), and the percentage of total variability due to heterogeneity ranged from 63.9% to 91.2% (for valvular disease and hypertension, respectively), supporting the use of a random-effects model. There was significant evidence of heterogeneity for all risk factors (Cochran Q ranging from 12.0 for valvular disease to 157.6 for hypertension; $P<.02$ for all risk factors), validating the choice of a random-effects model.

The AF risk score contributions were as follows: 3 points for the presence of heart failure, 2 points each for the presence valvular disease or

TABLE 1. Risk Factor Meta-analysis Summary

Risk factor	No. of patients included in analysis	Meta-analytic odds ratio (95% CI)[a]	AF risk score contribution
Heart failure[10-19]	65,074	3.6 (2.7-4.7)	3
Valvular disease[10,11,20,21]	14,880	2.4 (1.8-3.2)	2
Coronary artery disease[10-12,14,16,18-21]	57,516	2.1 (1.6-2.9)	2
Age (per 10 years)[10,12-14,16-18,20]	44,690	2.1 (1.9-2.4)	1 (aged 65-75 years) or 2 (aged >75 years)
Hypertension[10-23]	112,364	1.6 (1.4-1.9)	1
Diabetes mellitus[10,12-16,18,19,21,22,24]	69,739	1.6 (1.4-1.8)	1
Sex (male)[10,12-16,18,19,21,24,25]	63,164	1.5 (1.2-1.8)	1

[a]$P<.001$ for all.