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Short communication

Detection of atrial fibrillation in asymptomatic at-risk individuals

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ABSTRACT

Background: Undiagnosed atrial fibrillation (AF) exposes unsuspecting patients to elevated stroke risks. The optimal algorithm for identifying patients who should be screened for AF remains undetermined. The objective of this study is to determine the AF burden in an asymptomatic, at-risk population. We also sought to investigate potential predictors of undiagnosed AF.

Methods: This registry is a prospective observational study assessing continuous ECG monitoring in screening for AF using a wearable single lead 7-day continuous monitoring device. Patients included were asymptomatic individuals, at risk for AF as determined by either 1) ≥65 years of age with ≥1 high risk factor or; 2) ≥75 years of age and ≥2 moderate risk factors. A multivariable logistic regression was used to explore the predictive value of certain patient characteristics in identifying patients susceptible to have undiagnosed AF.

Results: Among the 942 patients included, 25 patients (2.7%) had evidence of AF detected. Only 8 patients had AF duration ≥24 h. History of perioperative AF (OR: 3.25, 95%CI: 1.08–9.79, $p = 0.036$), age over 85 (OR: 4.71, 95%CI: 1.31–16.92, $p = 0.017$) and absence of cardiovascular disease (CVD) (OR: 0.27, 95%CI: 0.10–0.76, $p = 0.013$) were found to be predictive of undiagnosed AF.

Conclusion: This study demonstrates the feasibility of office-based AF screening in at-risk population. The low rate of AF detection suggests that the optimal algorithm for identifying asymptomatic patients who would benefit from continuous screening remains unclear. Advanced age, history of perioperative AF and absence of CVD are variables that could be explored further.

1. Introduction

Atrial fibrillation (AF) is associated with a fivefold increase in the risk of stroke [1]. Anticoagulation is an effective therapy to minimize this risk [2]. However, the frequently paroxysmal and asymptomatic nature of AF has resulted in many patients remaining undiagnosed. Certain patient characteristics and medical history such as underlying comorbidities, advanced age or a history of perioperative AF are associated with a higher prevalence of AF. Emerging evidence suggests that the burden of AF coincides with stroke risks [3]. The intensity of monitoring also correlates with the likelihood of detecting the arrhythmia [4]; supporting a role for continuous monitoring in detecting AF. Efforts have been deployed to investigate various AF screening strategies and refine identification of patients at risk [5,6]. Yet, cost-effectiveness of stroke prevention AF screening programs remain prohibitive and optimization of the detection yield through improved stratification could encourage their adoption in routine medical care [7].

The objective of the present registry was to determine the AF burden in an asymptomatic at-risk population using an ambulatory continuous monitoring device. We also sought to investigate what patient characteristics could help predict which patients are most likely to have undiagnosed AF.

2. Methods

The AWARE AF registry is a prospective observational study assessing continuous ECG monitoring in screening for AF using a wearable single lead 7-day continuous monitoring device (Cardiostat,

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Table 1
Inclusion criteria and patient characteristics.

Characteristics	Total (N = 942)	No AF (N = 917, 97.3%)	AF (N = 25, 2.7%)	*p*
Age (years) mean ± std	78.7 ± 6.1	78.7 ± 6.1	80.4 ± 6.7	0.16
Gender Male (%)	545 (57.9)	536 (58.4)	9 (36.0)	0.025
Age ≥ 65 with history of either periop AF or CVA/TIA	272 (28.9)	261 (28.5)	11 (44.0)	0.09
Perioperative AF	68/272 (25.0)	63/261 (24.1)	5/11 (45.4)	0.15
CVA/TIA	207/272 (76.1)	200/261 (76.6)	7/11 (63.6)	0.30
Age ≥ 75 with at least any 2 of the followings:	699 (74.2)	683 (74.5)	16 (64.0)	0.24
Heart failure	98/699 (14.0)	96/683 (14.1)	2/16 (12.5)	1.0 (FE)
COPD or sleep apnea	113/699 (16.2)	111/683 (16.3)	2/16 (12.5)	1.0 (FE)
Hypertension	604/699 (86.4)	589/683 (86.2)	15/16 (93.8)	0.71 (FE)
Enlarged LA volume (>34 ml/m^2)	81/699 (11.6)	78/683 (11.4)	3/16 (18.8)	0.42 (FE)
Diabetes mellitus	287/699 (41.1)	278/683 (40.7)	9/16 (56.3)	0.21
LVEF <35%	17/699 (2.4)	17/683 (2.5)	0	1.0 (FE)
Chronic kidney disease	136/699 (19.5)	132/683 (19.3)	4/16 (25.0)	0.53 (FE)
Diastolic dysfunction (E/e$'$ > 14)	74/699 (10.6)	72/683 (10.5)	2/16 (12.5)	0.68 (FE)
CV disease	445/699 (63.7)	440/683 (64.4)	5/16 (31.3)	0.0064

Note: 38 patients had both inclusion criteria, ie Age ≥ 65 with history of either perioperative AF or CVA/TIA and Age ≥ 75 with ≥2 risk factors.
FE = Fisher's exact test (count <5).

Icentia, QC, Canada) in patients under the care of a cardiologist who provided consent. Patients included were asymptomatic individuals, in sinus rhythm, but at risk for AF as determined by either 1) ≥65 years of age with a history of either perioperative AF or stroke/transient ischemic attack (TIA) or; 2) ≥75 years of age and ≥2 of: heart failure, hypertension, diabetes, chronic kidney disease, chronic obstructive pulmonary disease/sleep apnea, cardiovascular disease (CVD), echocardiographic evidence of enlarged left atrium, left ventricular ejection fraction <35%, or significant diastolic dysfunction [8]. Exclusion criteria for both cohorts were prior diagnosis of AF on 12 lead ECG or Holter or, presence of ICD or pacemaker.

Group comparisons were performed with chi squared or Fisher's exact test or Kruskal-Wallis test as appropriate. A multivariable logistic regression was explored to determine the variables predictive of undiagnosed AF. Initially, 15 variables reflecting inclusion criteria were introduced in the full model: age, gender, perioperative AF, CVA/TIA, heart failure, COPD, hypertension, enlarged LA volume, diabetes, kidney disease, CV disease, diastolic dysfunction, enlarged right atrium, left ventricle hypertrophy and valvulopathy. We used a backward selection approach, with a 0.05 significance threshold to select the prognostic variables. The significant variables (Table 2) were used for adjustments in the final model. Our results were validated by testing a model including only variables that show association of $p < 0.10$ in the univariate analysis. All the statistical analysis were conducted using SAS 9.4 (SAS Institute, Cary, NC).

The program was conceived and coordinated by the Canadian Heart Research Centre (CHRC), a non-profit physician organization. The program was reviewed and approved by central ethics. No charges for ECG monitoring were made to public health insurance plans.

3. Results

The AWARE AF registry started recruitment in March of 2019 and stopped recruitment on December 31, 2019. In total, 942 patients were enrolled in 53 sites across Canada.

Mean age of the participants was 78.7 ± 6.1 years (16.8% were 65–74 years, 65.7% were 75–84 years and 17.5% were 85+ years old) and 58% were male. The inclusion criteria and related co-morbidities are summarized in Table 1. Interestingly, patients with AF were more likely to be women (64% vs 42%, $p = 0.025$),

The mean duration of monitoring was 6.8 ± 0.9 days. A total of 938 recordings were received and analysed: 25 patients (2.7%) had evidence of AF detected (95% CI: 1.6, 3.7%), 6 (24%) had mean AF duration of less than 5 min, 4 (16%) of 5–29 min, and 15 (60%) of 30 min or more. The mean heart rate during the episodes was 68 ± 13 bpm with a maximal and minimal mean rate of 141 ± 26 and 42 ± 9 bpm respectively. Among those patients with AF, duration of ≥24 h was detected in 8 patients (32%).

Table 2 shows the variables found to have a significant predictive value for any AF in the multivariable analysis which include: 1) age > 85 years (adjusted OR: 4.71, 95%CI: 1.31–16.92, p: 0.017) vs age 65–74; 2) prior CVD (adjusted OR: 0.27, 95%CI: 0.10–0.76, p: 0.013); and 3) history of perioperative AF (adjusted OR: 3.25, 95%CI: 1.08–9.79, p: 0.036), as the only significant variables. We also observed a significant effect of age when considered as a continuous variable (OR: 1.07; 95%CI: 1.01–1.14; p: 0.024). We validated these findings by testing an alternative model which also yielded the same three variables as predictive for undiagnosed AF.

4. Discussion

Asymptomatic patients managed by cardiologists maybe at risk for AF either because of prior medical history (perioperative AF or prior stroke) or because of a combination of advanced age and comorbidities or echocardiographic features. We found that only 2.7% of patients screened with a 7-day continuous monitoring had AF using our selection algorithm. These findings are consistent with prior findings but appear to be on the lower end of the reported range [9]. Other cohorts found higher detection rates when including symptomatic patients even with lower intensity monitoring; highlighting the importance of symptoms in predicting AF [10]. Possibly, a longer monitoring period or selection of even higher risk groups could have increased detection yield. However, a 7-day single lead continuous monitoring is practical with respect to patients' comfort.

While there is no specific minimal duration of AF that has been accepted as a threshold for anticoagulation, it is noteworthy that once AF was detected, only a third of the patients had AF duration of longer than 24 h; an important threshold. Future and ongoing studies will hopefully help further stratify stroke risks according to the AF burden in these patients.

A majority of the participants in this study were men. Thus, it can be surprising that newly identified AF was found predominantly in women. Gender differences in AF presentation and management are

Table 2
Multivariable model for predicting undiagnosed atrial fibrillation.

Variable	Adjusted odds ratio	95% Confidence interval	*p*-value
Age ≥ 85 years (65–74 reference)	4.71	1.31–16.92	0.017
History of Perioperative AF	3.25	1.08–9.79	0.036
Cardiovascular disease	0.27	0.10–0.76	0.013

well-documented [11]. Given the recent focus on the underdiagnosis and undertreatment of other cardiovascular diseases in women, the question as to whether AF in women is not as well recognized should be raised [12]. Despite the statistical non-significance of the gender variable in the multivariate analysis herein, it is important to note that our study lacks the power to adequately address this question.

Consistent with other studies, we found that age over 85 and a history of perioperative AF were important predictors of AF [2,13]. Surprisingly, the absence of CVD was also a predictor of undiagnosed AF despite being a known risk factor for AF. In an effort to validate this surprising finding, we also found that patients receiving beta-blockers, or antiplatelet drugs were less likely to be identified with undiagnosed AF. We would speculate that the CVD effect would be the result of the close follow-up that these patients receive. We suspect this would allow for earlier identification of AF in these patients who are known to be at higher risk. This may suggest that future screening research efforts could focus on patients who do not receive frequent cardiology care.

Our findings indicate that systematic screening of asymptomatic patients, even those with older age or additional co-morbid conditions and risk features may not be feasible since prevalence of AF appears to be low and the prevalence of high burden AF (>24 h in duration) is less than 0.7%.

4.1. Limitations

Our findings are limited by a small sample size, a duration of monitoring of only seven days, use of single channel technology and an unexpectedly low rate of AF detection. Importantly, the lower than expected event rate creates a risk of overfitting our multivariable regression model and further reduces the statistical power of our analyses; our results should be interpreted accordingly. The diverse inclusion criteria created a heterogeneous population, further limiting interpretation on the predictive value of any specific patient characteristic.

5. Conclusion

These results demonstrate the feasibility of cardiologist-office-based AF screening in at-risk population, using continuous ambulatory monitors. We found less than 3% prevalence of asymptomatic AF, raising questions about the usefulness of this approach for stroke prevention. Advanced age, a history of perioperative AF, and, absence of CVD could be explored as potential predictors of undiagnosed AF in future research.

Declaration of Competing Interest

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