New-onset Atrial Fibrillation in the Critically Ill

Atrial Fibrillation in the Critically Ill

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Online Data Supplement

Table of Contents

Methods

Study Population

From the bedside monitors, we observed the canonical vital signs—heart rate, respiratory rate, blood pressure, and oxygen saturation.

From the electronic data warehouse, we collected demographics, diagnosis codes, 12-lead ECG reports, procedures performed in the operating room, red blood cell transfusions, and the attributes pertaining to all outpatient and inpatient encounters including details such as clinic type, length of stay, and hospital mortality. We defined hemorrhage as three units of red blood cells transfused within a 24-hour period with no red blood cell transfusion in the preceding 24 hours.[23]

The UVa Clinical Data Repository (CDR) regularly collects information from the Virginia Department of Health's Division of Vital Records and Division of Health Statistics. From the CDR, we collected survival status and date of last known follow-up or death. The UVa Institutional Review Board approved this study with a waiver of informed consent.

Rhythm Classification

From the continuous ECG we made observations every 15 minutes of the preceding 30 minutes and calculated the mean interbeat or RR interval and the standard deviation or heart rate variability (HRV). We also calculated nonlinear dynamics of heart rate, namely, the coefficient of sample entropy (COSEn, a measure of irregularity),[19] the local dynamics score (LDs, a measure of reduced variability with interspersed ectopy),[20] and detrended fluctuation analysis (DFA, a measure of short-term correlations or ectopy).[24] As each measure is ECG-derived, failure to detect RR intervals led to a connected pattern of missing observations for all five measures (10.4%). Using only these five measures (mean RR, HRV, COSEn, LDs, DFA), we evaluated a previously validated rhythm classification methodology, developed from a large data set of 24-hour Holter studies.

Model Development

We studied 2,804 consecutive 24-hour Holter recordings collected by the University of Virginia Health System (UVa), an academic, tertiary-care center from December 2004 to October 2010. We previously reported the demographic and clinical characteristics of these patients[1] and also described the development and validation of rhythm classification algorithms in this and publicly available data sets to distinguish atrial fibrillation from sinus rhythm and sinus rhythm with ectopy using measurements of the linear and nonlinear domains of interbeat interval time series.[2-4] We subdivided the interbeat interval time series into 377,285 10-minute segments and classified them into one of two mutually exclusive categories: (1) *AF* if the burden of AF or atrial flutter (AFL) was greater than 5% (i.e. ≥ 30 seconds) or (2) *not AF*, which was primarily comprised of sinus rhythm with varying degrees of ectopy. The heart rate metrics for each 10-minute segment included the means, standard deviations, COSEn, DFA, and LDs. We then developed a random forest model to detect AF using only these ECG-derived measurements. We report the performance of a forest containing 100 tress that had maximal performance as tested on a random sample (20%) held out from the original development data set.

External Validation

We performed external validation of the model in our intensive care unit (ICU) data set on 500 randomly sampled segments of ECG tracings, each of 30 minutes duration. We annotated each for the presence of AF or AFL, including both the time of onset and duration. We evaluated the algorithm on segments consisting of ≥ 10 minutes of continuous rhythm, consistent with the data structure used in model development.[3]

Propensity Score Matching

Propensity score matching enables parametric models for causal inference to work better by selecting well-matched subsets of the original case and control groups.[5] We constructed a propensity score to balance patient characteristics between groups of patients with and without AF during their ICU stay by fashioning a multiple logistic regression model to predict the probability of any AF during ICU monitoring controlling for all listed covariates, including demographics, acute and chronic comorbidities, and postoperative status as listed in **Online Table 5**. We then matched each patient admission with AF to one without using a nearest neighbor method without replacement. Admissions with scores above the maximum or below the minimum of the comparator group were discarded (33 controls, 11 cases).

Results

AF Detection Algorithm Performance

In the testing subset held out from the development data set, the model demonstrated excellent performance with a sensitivity of 96% and PPV of 99% (**Online Table 1**). In the validation set of 500 randomly sampled segments from ICU admissions, the model also performed well with a sensitivity of 89% and PPV of >99% (**Online Table 2**).

Propensity Score Matching

Of the 1610 admissions with AF, 1594 (99%) were successfully matched to admissions without AF. The matching resulted in greater balance in covariates between the two groups (**Online Table 5**).

Tables

Online Table 1: Confusion Matrix of Model Evaluated on Test Set from Holter dataset

		Reference	
		AF	**Other**
Prediction	**AF**	5,698	41
	Other	251	69,463

N=75,456 observations of 10 minute electrocardiography segments randomly selected from 2,801 unique 24-hour Holter studies; Accuracy: 99.6% (95% CI: 99.6-99.7%); Sensitivity: 95.7%; Specificity: 99.9%; Positive Predictive Value: 99.3%; Negative Predictive Value: 99.6%; Prevalence: 7.9%; Detection Rate: 7.6%. AF: atrial fibrillation or atrial flutter; Other: all other cardiac rhythms.

Online Table 2: Confusion Matrix of Model Externally Validated on Sample from ICU dataset

		Reference	
		AF	**Other**
Prediction	**AF**	46	0
	Other	6	415

N=495 observations of individually verified 10-30 minute electrocardiography segments, randomly selected from both the medical and surgical intensive care units (while 500 segments were randomly selected, not all contained ≥ 10 minutes of continuous cardiac rhythm due to artifact or missing data). Accuracy: 98.7% (95% CI: 97.2-99.5%); Sensitivity: 89%; Specificity: >99%; Positive Predictive Value: >99%; Negative Predictive Value: 98.6%; Prevalence: 11.1%; Detection Rate: 9.9%. AF: atrial fibrillation or atrial flutter; Other: all other cardiac rhythms.

Online Table 3: Baseline characteristics and outcomes by category

	No AF	New Subclinical AF	New Clinical AF	Prior AF
Percentage (n)	74 (6,222)	7 (626)	1 (123)	17 (1,385)
Demographics				
Age, years	56 (45-67)	59 (46-72)	69 (61-78)	72 (63-80)
Male	55 (3,440)	61 (381)	50 (61)	60 (835)
Body mass index	27 (22-33)	27 (22-33)	28 (24-33)	28 (23-34)
Number of prior office visits	0 (0-1)	0 (0-1)	0 (0-1)	1 (0-6)
Number of recent office visits	0 (0-1)	0 (0-1)	0 (0-1)	0 (0-4)
Number of prior 12-lead ECGs	1 (0-3)	1 (0-3)	1 (0-3)	2 (0-10)
Severity of Illness				
OASIS	26 (21-32)	30 (24-36)	32 (28-38)	30 (24-36)
Number of vasopressors required in first 24 hours	0 (0-0)	0 (0-1)	0 (0-1)	0 (0-1)
Atrial fibrillation				
ICU monitoring data, days	1.3 (0.7-2.6)	3.7 (1.7-8.8)	6.0 (3.2-12.3)	2.2 (1.0-4.7)
Detected during ICU stay	0 (0)	100 (626)	100 (123)	62 (861)
Time to onset from start of ICU monitoring, hours	0 (0-0)	35 (11-93)	35 (14-87)	5.5 (0-36)
Cumulative duration, minutes	0 (0-0)	45 (30-105)	270 (75-728)	90 (0-1095)
Burden as percentage	0 (0-0)	0.7 (0.3-2.2)	2.7 (0.9-12.7)	1.8 (0-50.0)
New atrial fibrillation diagnosis code at hospital discharge	2 (107)	0 (0)	73 (90)	9 (120)
New atrial flutter diagnosis code at hospital discharge	0 (18)	0 (0)	11 (14)	2 (28)

12-lead ECG confirmation of new AF/AFL in follow-up	0 (0)	7 (44)	67 (83)	5 (76)
Days to 12-lead ECG confirmation of new AF/AFL	0 (0)	143.5 (31.7-423.3)	1.5 (0.1-3.1)	2.3 (0.2-13.7)
Final ICU rhythm AF/AFL	0 (0)	3 (20)	13 (16)	18 (213)
CHA_2DS_2-VASc	2 (1-3)	2 (1-4)	4 (2-5)	4 (3-5)
CHA_2DS_2-VASc ≥ 2	60 (3,715)	66 (414)	85 (105)	92 (1,277)
Comorbid conditions				
Acute kidney injury	15 (960)	23 (142)	27 (33)	28 (390)
Acute myocardial infarction	5 (287)	8 (48)	13 (16)	13 (180)
Acute respiratory failure	26 (1,640)	50 (316)	69 (85)	45 (630)
Coronary artery disease	22 (1,399)	29 (181)	40 (49)	52 (725)
Chronic kidney disease	19 (1,161)	23 (147)	22 (27)	38 (523)
Cardiomyopathy	4 (230)	5 (31)	7 (8)	15 (206)
Conduction disorder	8 (473)	9 (56)	12 (15)	22 (307)
Ischemic stroke	9 (532)	11 (71)	12 (15)	16 (218)
Diabetes mellitus	30 (1,865)	31 (195)	36 (44)	47 (651)
History of atrial fibrillation	0 (0)	0 (0)	0 (0)	81 (1128)
History of atrial flutter	0 (0)	0 (0)	0 (0)	11 (150)
Heart failure	13 (805)	18 (115)	24 (29)	49 (678)
Hemorrhage	7 (440)	14 (87)	15 (18)	8 (116)
Hyperlipidemia	38 (2,349)	40 (248)	43 (53)	61 (844)
Hypertension	60 (3,719)	64 (401)	77 (95)	85 (1,175)
Hyperthyroidism	1 (84)	2 (12)	2 (2)	2 (34)
Obstructive sleep apnea	12 (749)	15 (94)	9 (11)	23 (314)
Pulmonary embolism	4 (219)	5 (30)	7 (9)	3 (45)
Pulmonary hypertension	5 (338)	7 (43)	9 (11)	20 (282)
Post-operative state	40 (2,458)	42 (265)	53 (65)	31 (435)

Chronic pulmonary disease	17 (1,066)	27 (168)	24 (30)	33 (461)
Sepsis	21 (1,304)	40 (251)	50 (61)	40 (563)
History of tobacco use	34 (2,109)	35 (217)	30 (37)	22 (310)
Valvular heart disease	5 (330)	4 (27)	7 (8)	20 (275)
Hospital Outcomes				
Hospital LOS, days	7 (4-12)	11 (6-21)	16 (10-25)	8 (5-16)
ICU LOS, days	1.8 (1.0-3.4)	4.5 (2.1-10.1)	7.4 (3.9-14.5)	2.8 (1.4-5.7)
Hospital mortality	8 (468)	16 (98)	32 (39)	18 (253)

Values are percentage (counts) or median (interquartile range). ICU: intensive care unit; ECGs: electrocardiograms; OASIS: Oxford Acute Severity of Illness Score; LOS: length of stay.

Online Table 4: Physiological measurements during periods of atrial fibrillation by category

	New Subclinical AF	New Clinical AF	Prior AF	p-value
Heart rate	94 (82-107)	102 (90-116)	98 (86-111)	<0.001
Respiratory rate	21 (17-26)	22 (19-26)	21 (17-26)	<0.001
Oxygen Saturation	97 (95-99)	97 (95-98)	97 (96-99)	<0.001
Systolic Blood Pressure	119 (104-139)	113 (101-127)	113 (100-129)	<0.001
Diastolic Blood Pressure	65 (57-74)	62 (54-72)	64 (57-73)	<0.001

Heart rate in beats per minute; respiratory rate in breaths per minute; oxygen saturation in percent from pulse oximetry; systolic and diastolic blood pressures in millimeters of mercury.

Online Table 5: Summary of covariates before and after propensity score matching

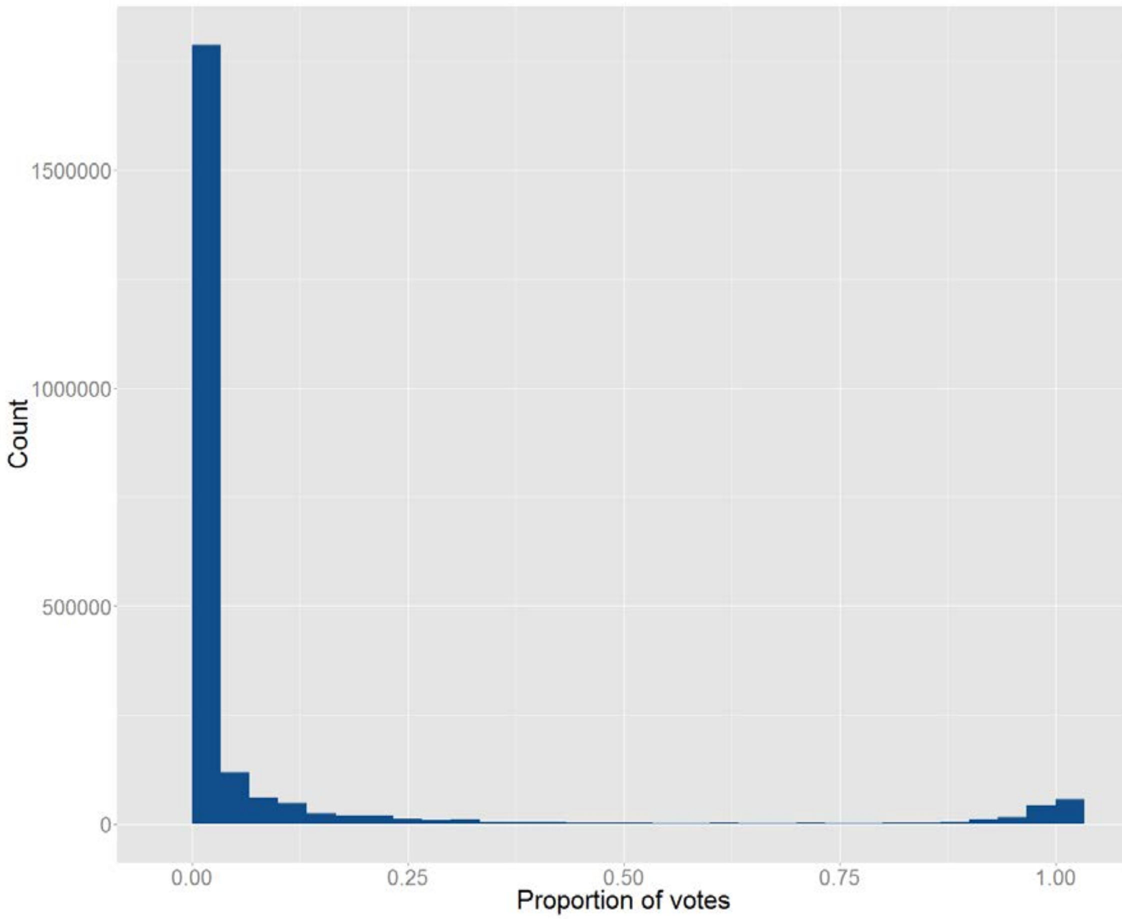
	Before Matching			*After Matching*		
	Any AF (n: 1610)	**No AF (n: 6746)**	**Std. Mean Diff.**	**Any AF (n: 1594)**	**No AF (n: 1594)**	**Std. Mean Diff.**
Distance	0.307	0.165	0.816	0.304	0.298	0.030
Age (years)	66.2	56.1	0.610	66.1	65.3	0.047
Female	0.404	0.443	-0.079	0.407	0.415	-0.017
Body Mass Index	28.2	27.3	0.066	28.2	28.3	0.001
Acute Kidney Injury	0.276	0.160	0.258	0.272	0.275	-0.004
Acute Myocardial Infarction	0.117	0.051	0.207	0.118	0.112	0.018
Acute Respiratory Failure	0.521	0.272	0.498	0.517	0.533	-0.031
Coronary Artery Disease	0.414	0.250	0.332	0.411	0.403	0.017
Chronic Kidney Disease	0.306	0.202	0.225	0.305	0.310	-0.011
Cardiomyopathy	0.087	0.050	0.132	0.087	0.083	0.016
Conduction Abnormality	0.139	0.093	0.133	0.140	0.133	0.012
Ischemic Stroke	0.135	0.092	0.128	0.135	0.138	-0.011
Diabetes Mellitus	0.394	0.314	0.164	0.393	0.402	-0.018
Heart Failure	0.353	0.157	0.410	0.348	0.337	0.024
Hyperlipidemia	0.506	0.397	0.217	0.504	0.503	0.001
Hypertension	0.760	0.618	0.334	0.760	0.747	0.031
Hyperthyroidism	0.021	0.015	0.041	0.021	0.019	0.009
Obstructive Sleep Apnea	0.174	0.132	0.112	0.173	0.171	0.007
Pulmonary Embolism	0.041	0.035	0.030	0.041	0.043	-0.006
Pulmonary Hypertension	0.143	0.066	0.220	0.140	0.132	0.023
Postoperative State	0.390	0.385	0.011	0.390	0.372	0.036

Chronic Pulmonary Disease	0.301	0.184	0.254	0.299	0.298	0.001
Sepsis	0.445	0.217	0.458	0.441	0.451	-0.020
Tobacco Use	0.262	0.334	-0.163	0.262	0.268	-0.013
Valvular Heart Disease	0.125	0.065	0.181	0.121	0.114	0.023
Hemorrhage	0.122	0.069	0.162	0.119	0.126	-0.023
OASIS	31.4	27.2	0.489	31.3	31.4	-0.013
Vasopressors	0.476	0.209	0.303	0.458	0.450	0.009

Values are proportion or standardized mean difference (Std.Mean Diff.) unless otherwise noted. AF: atrial fibrillation.

Figures

Online Figure 1. Distribution of estimated probability of atrial fibrillation as determined by rhythm classification model.



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