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ORIGINAL ARTICLE

Artificial Intelligence Model Predicts Sudden Cardiac Arrest Manifesting With Pulseless Electric Activity Versus Ventricular Fibrillation

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BACKGROUND: There is no specific treatment for sudden cardiac arrest (SCA) manifesting as pulseless electric activity (PEA) and survival rates are low; unlike ventricular fibrillation (VF), which is treatable by defibrillation. Development of novel treatments requires fundamental clinical studies, but access to the true initial rhythm has been a limiting factor.

METHODS: Using demographics and detailed clinical variables, we trained and tested an AI model (extreme gradient boosting) to differentiate PEA-SCA versus VF-SCA in a novel setting that provided the true initial rhythm. A subgroup of SCAs are witnessed by emergency medical services personnel, and because the response time is zero, the true SCA initial rhythm is recorded. The internal cohort consisted of 421 emergency medical services-witnessed out-of-hospital SCAs with PEA or VF as the initial rhythm in the Portland, Oregon metropolitan area. External validation was performed in 220 emergency medical services-witnessed SCAs from Ventura, CA.

RESULTS: In the internal cohort, the artificial intelligence model achieved an area under the receiver operating characteristic curve of 0.68 (95% CI, 0.61–0.76). Model performance was similar in the external cohort, achieving an area under the receiver operating characteristic curve of 0.72 (95% CI, 0.59–0.84). Anemia, older age, increased weight, and dyspnea as a warning symptom were the most important features of PEA-SCA; younger age, chest pain as a warning symptom and established coronary artery disease were important features associated with VF.

CONCLUSIONS: The artificial intelligence model identified novel features of PEA-SCA, differentiated from VF-SCA and was successfully replicated in an external cohort. These findings enhance the mechanistic understanding of PEA-SCA with potential implications for developing novel management strategies.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: artificial Intelligence ■ cardiovascular diseases ■ emergency medical services ■ stroke ■ ventricular fibrillation

See Editorial by Tereshchenko

Despite significant advances in the prevention and treatment of cardiovascular disease, sudden cardiac arrest (SCA) is an important mode of death worldwide, accounting for more years of potential life lost than any individual cancer.[1,2] Improvements in emergency medical services (EMS) response and acute

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WHAT IS KNOWN?

- Treatment of sudden cardiac arrest (SCA) has long been based on the defibrillation of shockable rhythm (ventricular fibrillation, VF), but there is no specific treatment for SCA manifesting as pulseless electric activity (PEA) for which survival rates are much lower than in VF.
- A small subset of PEA-SCA can be successfully resuscitated and ultimately survive. Further increments in survival await the ability to predict which SCAs will manifest as PEA versus VF with the goal of improving mechanistic understanding of PEA.
- Toward this purpose, published studies are limited by the inability to access the initial SCA presenting rhythm; due to the time elapsed in responding to a 911 call, the first recorded rhythm in most SCAs may not be the actual initial rhythm.

WHAT THE STUDY ADDS

- We obtained the initial rhythms using a novel approach of analyzing recordings and data from the subset of SCAs that were witnessed by emergency medical services providers.
- We trained and tested an AI model that identified novel determinants of initial rhythms, including anemia, older age, higher weight, and prearrest dyspnea for PEA; and previously diagnosed coronary artery disease, prearrest chest pain, and young age for VF.
- These findings have contributed to the mechanistic understanding of PEA and may help to predict which individuals at increased risk of SCA will present with PEA versus VF.

Nonstandard Abbreviations and Acronyms

AI	artificial intelligence
AUC	area under the receiver operating characteristic curve
CAD	coronary artery disease
EMS	emergency medical services
PEA	pulseless electric activity
SCA	sudden cardiac arrest
SHAP	Shapley Additive Explanations
VF	ventricular fibrillation
XGBoost	extreme gradient boosting decision tree model

management have had a positive impact on survival outcomes, but average rates of survival to hospital discharge in the United States remain in the range of 10%.[3,4]

Forty years ago, shockable rhythms (ventricular fibrillation, VF) dominated, accounting for 70% to 80% of SCAs.[5] However, the proportions have shifted over time, and nonshockable rhythms (pulseless electric activity, PEA/asystole) now account for 70% to 80% of the cases.[6–9] This phenomenon has implications for overall survival from SCA because VF and PEA have divergent survival outcomes: VF is potentially treatable with defibrillation and displays significantly better outcomes following resuscitation compared with PEA for which there are no specific therapeutic measures and survival remains poor (≈30% versus 5% survival to discharge from hospital).[3] Given these profound differences in the treatment and prognosis of PEA and VF, an understanding of the clinical profile of each group could provide new mechanistic insights leading to the development of novel PEA management and therapeutics.

Previous studies have attempted to distinguish clinical profiles of individuals presenting with PEA versus VF, but these utilized the presenting rhythm recorded by EMS personnel after a response delay.[10,11] Following a 911 call, it can take 6 to 10 minutes for EMS to arrive, and during this time delay, the initial rhythm may change to a different rhythm. It is conceivable, for example, that an initial rhythm of VF could spontaneously convert to PEA or asystole.[12,13] The inability to study the true initial rhythm has long been a barrier to studies in this field.

A small but distinct subgroup of individuals suffers their SCA event in the presence of EMS personnel. because there is virtually no time delay in this setting, the true SCA initial rhythm has been recorded.[14] We hypothesized that evaluation of the initial rhythm from EMS-witnessed SCA cases will provide a more relevant and accurate model for distinguishing PEA from VF. Therefore, we investigated EMS-witnessed SCA cases from 2 prospective community-based SCA cohorts to train and test an artificial intelligence (AI) model that would distinguish between SCA victims presenting with PEA versus VF.

METHODS

All analytical methods are included in this article. The data are not publicly available but deidentified data and code will be made available upon reasonable request.

Study Population

The study samples are drawn from the Oregon SUDS (Oregon Sudden Unexpected Death Study) and the Ventura PRESTO study (Ventura Prediction of Sudden Death in Multi-ethnic Communities). Study protocols have been described earlier in more detail.[15,16] Briefly, both studies are ongoing, prospective, community-based studies of out-of-hospital SCA and use an identical design. Oregon SUDS has prospectively enrolled out-of-hospital SCA since 2002 in the Portland, Oregon metropolitan area (population ≈1 million) and Ventura PRESTO since 2015 in Ventura County, California (population ≈850 000). Potential out-of-hospital SCA cases are identified in collaboration with the region's 2-tiered EMS system, regional hospitals, and the

state Medical Examiner's office. Using an established adjudication methods to identify SCA of likely cardiac cause, all available EMS reports, medical records, medical examiner's reports, death certificates, and autopsy reports are obtained and reviewed. SCA cases with likely noncardiac etiology (eg, trauma, overdose, stroke) or chronic terminal illness are excluded.

Study Subjects

In the present study, we included cases of patients aged 18 and older from the Oregon SUDS and the Ventura PRESTO studies whose SCA was witnessed by EMS personnel and who had either PEA or VF as the initial rhythm. Because pulseless ventricular tachycardia cases were a minority of the shockable rhythms (VF/ventricular tachycardia; 26%) and are also treated by defibrillation, these were included in the VF subgroup. For the Oregon SUDS, SCA cases were prospectively ascertained between 2002 and 2022, whereas for the Ventura PRESTO study, SCA cases were prospectively ascertained between 2015 and 2022. Information on demographics and prearrest clinical characteristics was obtained by evaluation of lifetime medical records, which were obtained from regional health care systems and used to characterize the detailed clinical profile. We included information on prearrest clinical characteristics if the patient provided written consent or was deceased, in which case consent was waived. Information on prearrest warning symptoms was obtained from EMS reports.

Institutional review boards of Ventura County Medical Center, Oregon Health and Science University, Cedars-Sinai Health System, and all other health systems and participating hospitals approved the study protocol.

Supervised Machine Learning

Extreme gradient boosting decision tree models (XGBoost, Version 1.3.3)[17] were built for the binary classification of either PEA or VF. The Microsoft Fast and Lightweight AutoML Library (Version 1.0.14)[18] was used to automate and optimize hyperparameter search and selection. XG boost provides Ensemble boosting, tunable regularization parameters, and model explainability. XGBoost is demonstrated to be a strong baseline model in predictive health care machine learning applications such as breast cancer survival[19] and mortality from myocardial infarction.[20] All validations were also repeated using logistic regression models and are available in the Supplemental File for direct comparison to a more traditional, nonboosted approach.

10-fold cross-validation was performed within the Oregon SUDS data set to validate the automated hyperparameter selection criteria and model performance in the internal cohort. In each fold, unique splits (80% training, 10% validation, 10% test) were utilized such that across all folds, all internal patients were utilized in the test set exactly once. A final model was built using a split (90% training, 10% validation) from the Oregon SUDS data to maximize the final training sample size.

For external validation, the final model developed exclusively in the Oregon SUDS cohort, as described above, was applied directly to the previously unseen Ventura PRESTO dataset.

Feature importance analysis was performed using 2 methods. First, the built-in XGBoost feature importance function was used to compare the absolute information gain from all input variables to the trained model. Additionally, SHapley Additive exPlanations (SHAP)[21] were used to analyze test-wise feature influences during model inference using a game-theoretical approach. Both of these approaches allow group analysis and derivation of key features driving the prediction of individual cases. Individual patient feature importance plots were created as described in our previous work.[22]

Data Preprocessing

All variables with >20% missingness in the internal cohort were dropped from the analysis to avoid missing-data bias. Final input data included 56 variables which were categorized into 4 groups: demographics (5), medical history (37), medications (4), and prearrest symptoms (10). All included variables are presented in Supplemental Table 1. The remaining missing values were imputed using the median for continuous variables and the mode for categorical variables. There were no missing values for PEA/VF, so no imputation was performed for these variables. Data normalization before model training and validation is not required for XGBoost. The AI model was evaluated with 2 sets of input data: (1) demographic variables only and 2) all variables.

Statistical Methods

The area under the receiver operating characteristic curve (AUC) was used to evaluate model predictive performance across all possible sensitivity-specificity thresholds. 95% CIs for AUC curves were generated using bootstrapping with 1000 iterations. The DeLong test was used to determine the *P* value significance between AUC curves. Youden J statistic was used to identify an optimal cutoff threshold for the probabilistic predictions of trained models. Brier score was used to evaluate the accuracy of probabilistic predictions and to compare model calibration. All models and AI analyses were generated using Python Version 3.7.11. Further analysis was performed using R Version 4.1.1, for which statistical significance was assessed using Mann-Whitney *U* test Wilcoxon, Kruskal-Wallis rank sum, or Pearson's χ^2 test. Continuous variables are presented as mean (SD).

RESULTS

Subject Characteristics

The internal cohort included 421 EMS-witnessed SCA cases from Oregon SUDS, of which 249 had PEA and 172 had VF as the initial rhythm. The external SCA cohort (Ventura PRESTO) included 220 EMS-witnessed SCA cases, of which 170 had PEA and 50 had VF as the initial rhythm. The study sample constituted 8.2% of all SCA cases from Oregon SUDS and Ventura PRESTO. Cases in Ventura PRESTO were older in comparison to Oregon SUDS cases (72.3 [14.4] versus 67.5 [15.0] years; $P<0.001$), but there was no difference in sex distribution (65.0% and 61.5% males, respectively; $P=0.44$). The proportion of White Non-Hispanic individuals was higher in Oregon SUDS (78.6% versus 63.6%), whereas the proportion of Hispanic individuals was higher in Ventura PRESTO (25.9% versus 1.4%) ($P<0.001$). Median height was similar in Ventura PRESTO and Oregon

SUDS (170.3 [9.2] versus 170.7 [12.7] cm, respectively; *P*=0.24), but cases in Oregon SUDS had higher median weight (92.1 [31.2] versus 85.9 [25.9] kg; *P*=0.008). Demographics, clinical characteristics and initial rhythms are presented in Table 1.

There was no significant difference in the prevalence of previously diagnosed coronary artery disease (CAD; overall prevalence 53.4%), anemia (40.1%), chronic kidney disease; 41.7%), diabetes (38.4%), asthma (8.1%), chronic obstructive pulmonary disease; 18.2%), heart failure (30.3%), atrial fibrillation/flutter (28.4%), cancer (14.8%), prior implantable cardioverter defibrillator implantation (4.8%), sleep apnea (12.3%), peripheral vascular disease (12.6%), cardiomyopathy (11.8%), seizure disorder (4.6%), prior SCA (0.5%), or schizophrenia (0.6%) between Ventura PRESTO and Oregon SUDS cases, respectively. The prevalence of mood disorder (25.6% versus 14.5%; *P*=0.002), and prearrest chest pain (34.7% versus 20.0%; *P*<0.001) was higher in Oregon SUDS, while cases in Ventura PRESTO were more likely to have prearrest weakness (17.4% versus 9.0%; *P*=0.005) and a prior pacemaker (14.6% versus 8.3%; *P*=0.03).

Model Performance

In the internal dataset (Oregon SUDS), the AI model achieved an AUC of 0.52 (95% CI, 0.44–0.60) with only demographic variables. The model performance increased to an AUC value of 0.68 (0.61–0.76; *P*<0.001; Delong test) when clinical variables were added. The model performance was similar in the external cohort (Ventura PRESTO), achieving an AUC of 0.56 (0.44–0.68) with demographics and an AUC of 0.72 (0.590.84) when clinical variables were added to demographics (*P*=0.003; Delong test). Model performance metrics and AUC curves in the internal and external cohorts are presented in Table 2; Figure 1. Brier score calibration of All Data models and Demographics Data models in the internal cross-validation (Oregon SUDS) and external validation (Ventura PRESTO) cohorts are presented in Table S2. Lower brier scores for the All Data models in both internal and external validation compared with the Demographics Data models indicate improved calibration of probabilistic performance for the All Data models. Logistic regression models had similar performance to the AI model in both internal and external cohorts (Table 3).

Table 1. Characteristics of Individuals With Sudden Cardiac Arrest (SCA) According to Study Site and Initial Rhythm

	Oregon SUDS			Ventura PRESTO		
Characteristic	PEA (n=249)	VF (n=172)	p-value	PEA (n=170)	VF (n=50)	*P* value
Age, y; median (IQR)	68 (59–79)	67 (56–76)	0.044	76 (65–84)	68 (56, 76)	0.001
Male sex, n (%)	147/249 (59%)	112/172 (65%)	0.2	103/170 (61%)	40/50 (80%)	0.018
Height, cm; median (IQR)	173 (163–177)	175 (165–178)	0.11	170 (163–177)	172 (167–178)	0.15
Weight, kg; median (IQR)	90 (70, 108)	86 (70–102)	0.8	82 (68–100)	84 (74–104)	0.10
Prior CAD, n (%)	104/249 (42%)	126/172 (73%)	<0.001	77/170 (45%)	35/50 (70%)	0.004
Anemia, n (%)	110/243 (45%)	53/171 (31%)	0.005	77/164 (47%)	12/50 (24%)	0.007
Chest pain, n (%)	50/222 (23%)	81/156 (52%)	<0.001	21/149 (14%)	18/46 (39%)	<0.001
Dyspnea, n (%)	109/213 (51%)	62/154 (40%)	0.050	68/145 (47%)	18/45 (40%)	0.5
Diaphoresis, n (%)	16/213 (7.5%)	27/154 (18%)	0.005	22/145 (15%)	7/45 (16%)	>0.9
Anti-depressants, n (%)	74/196 (38%)	36/148 (24%)	0.011	36/141 (26%)	7/38 (18%)	0.5
CKD, n (%)	107/243 (44%)	58/171 (34%)	0.049	81/164 (49%)	16/50 (32%)	0.045
Cardiomyopathy, n (%)	18/223 (8.1%)	26/163 (16%)	0.025	17/147 (12%)	7/45 (16%)	0.7
β-Blockers, n (%)	91/196 (46%)	67/148 (45%)	>0.9	69/141 (49%)	16/38 (42%)	0.6
Mood disorder, n (%)	68/243 (28%)	38/171 (22%)	0.2	28/164 (17%)	3/50 (6.0%)	0.086
PVD, n (%)	38/243 (16%)	18/171 (11%)	0.2	19/164 (12%)	4/50 (8.0%)	0.6
Congestive heart failure, n (%)	72/249 (29%)	61/172 (35%)	0.2	50/170 (29%)	11/50 (22%)	0.4
Cancer, n (%)	32/243 (13%)	29/171 (17%)	0.4	26/164 (16%)	6/50 (12%)	0.7
Sleep apnea, n (%)	29/243 (12%)	24/171 (14%)	0.6	22/164 (13%)	2/50 (4.0%)	0.11
Nausea/vomiting, n (%)	24/222 (11%)	27/156 (17%)	0.10	13/149 (8.7%)	9/46 (20%)	0.078
Afib/Aflutter, n (%)	59/220 (27%)	50/162 (31%)	0.5	35/145 (24%)	18/43 (42%)	0.038
Prior ICD, n (%)	6/223 (2.7%)	12/163 (7.4%)	0.057	9/147 (6.1%)	1/45 (2.2%)	0.5

Afib indicates atrial fibrillation; Aflutter, atrial flutter; CAD, coronary artery disease; CKD, chronic kidney disease; ICD, implantable cardioverter defibrillator; IQR, interquartile range; Oregon SUDS, Oregon Sudden Unexpected Death Study PEA, pulseless electric activity; PVD, peripheral vascular disease; Ventura PRESTO, Prediction of Sudden death in Multi-ethnic Communities; and VF, ventricular fibrillation.

Table 2. Model Performance in the Internal and External Data Sets

Model	AUC (95% CI)	Youden J statistic threshold	Sensitivity (95% CI)	Specificity (95% CI)
Internal cohort				
Demographics	0.521 (0.442–0.600)	0.415	0.564 (0.477–0.652)	0.467 (0.376–0.558)
All variables	0.684 (0.610–0.758)	0.381	0.634 (0.552–0.715)	0.634 (0.549–0.718)
External cohort				
Demographics	0.562 (0.440–0.684)	0.409	0.740 (0.599–0.882)	0.366 (0.263–0.470)
All variables	0.717 (0.591–0.843)	0.384	0.743 (0.605–0.880)	0.653 (0.554–0.752)

AUC indicates area under the receiver operating characteristics curve..

Key Predictors

To understand the key variables in the AI model that distinguish PEA from VF, feature importance is shown in Figure 2 (all features with importance >0 in the external cohort) and Figure S1 (all features in the internal and external cohorts). Based on the built-in XGBoost feature importance, the most important variables were chest pain, previously diagnosed CAD, pre-arrest diaphoresis, history of anemia, pre-arrest dyspnea, and age (both in the internal and external cohort). Other less important clinical variables were, for example, antidepressant medications, weight, height, chronic kidney disease, cardiomyopathy, mood disorder, and β-blocker medication, while sex, diabetes, antipsychotic medications, chronic obstructive pulmonary disease, asthma, or prior SCA had no importance in the external cohort.

By the SHAP analysis, the presence of anemia and older age were the most important determinants of PEA, while CAD, chest pain, and young age were the most important determinants of VF. The magnitude and direction of the 4 most important features (CAD, chest pain, anemia, and age) were similar in men and women. Moreover, increased weight predicted PEA, whereas increased height predicted VF. SHAP values are presented in Figures 3 and 4. SHAP plots of the demographics-only model are presented in Supplemental Figures S2 and S3. Examples of waterfall plots for a PEA and a VF case are also presented in Figure 5. The prevalence of key predictors according to study site and initial rhythm are presented in Table 1. The prevalence of less important features according to study site and initial rhythm are shown in Table S4.

DISCUSSION

To our knowledge, this is the first report of an algorithm that has identified clinical determinants of PEA versus VF

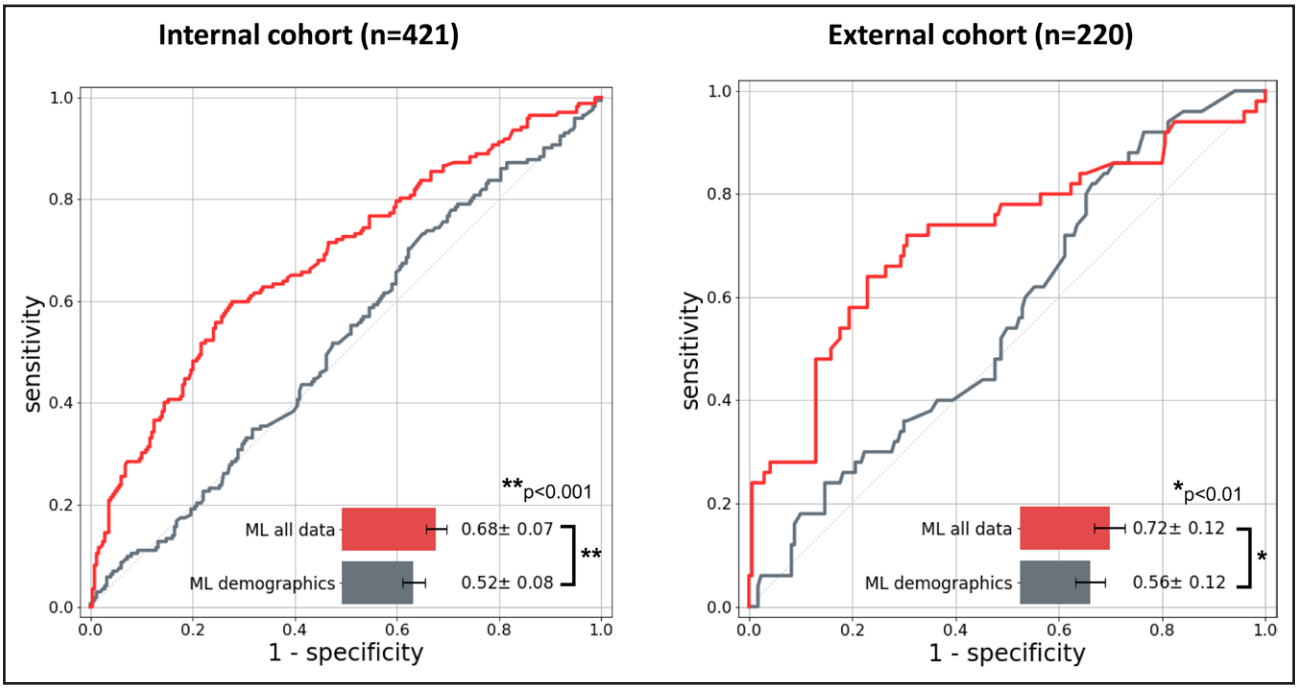

Figure 1. Receiver operating curves distinguishing pulseless electric activity (PEA) from ventricular fibrillation (VF) in the internal and external cohorts.
ML indicates machine learning.

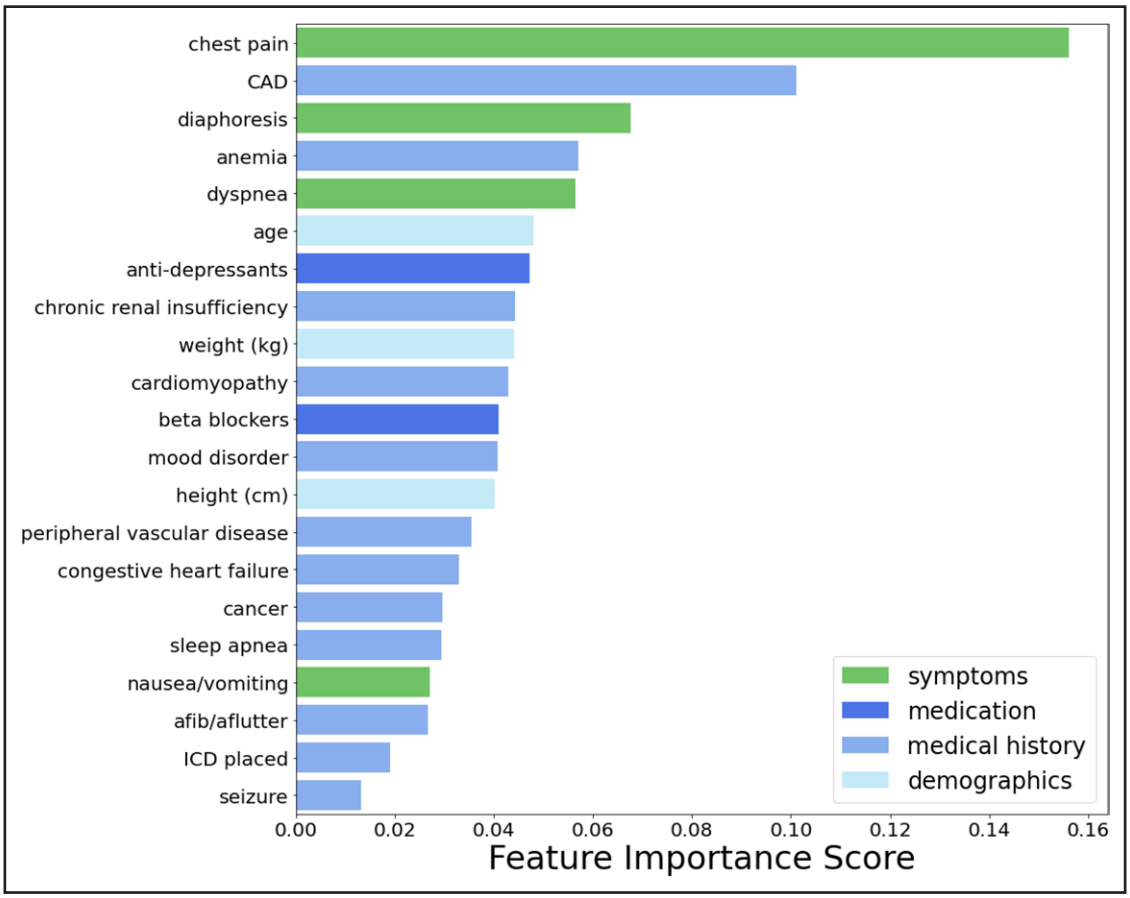

Figure 2. Feature importance in the external cohort according to the in-built XGBoost function.
Afib indicates atrial fibrillation; Aflutter, atrial flutter; CAD, coronary artery disease; and ICD, implantable cardioverter defibrillator.

in EMS-witnessed SCA cases, a novel setting that makes evaluation of the initial rhythm feasible. Although only a small proportion of out-of-hospital SCA cases are witnessed by EMS personnel, this subgroup is unique due to the absence of delay in the first ECG recording. The use of this novel approach provided reliable information regarding initial SCA rhythms, generally not feasible to obtain for the majority of SCA victims. Prospective ascertainment of all out-of-hospital SCA cases from 2 US communities conducted over 20 years allowed for the collection of a feasible number of EMS-witnessed SCA cases. The AI model was successfully validated in the external cohort. The most important features separating PEA and VF were CAD, chest pain, anemia, and age, for both sexes. These results improve the understanding of mechanistic differences between PEA and VF, representing a first step to work toward novel PEA therapies. These findings also have the potential to better identify which individuals at high risk of SCA will present with PEA versus VF, but due to the moderate performance of the model, further investigation is required before clinical utilization.

A major advantage of using AI techniques in comparison to conventional statistical tools is that these require fewer assumptions about data structure, and hence AI can be especially useful for the analysis of complex nonlinear relationships. In comparison to conventional methods, AI models can potentially identify novel patterns of variables that may contribute to PEA-SCA versus VF-SCA. We have previously reported differences between overall PEA and VF cases in the Oregon SUDS,[11] but we did not have access to the initial presenting rhythm, only the first rhythm recorded by EMS personnel when they arrived at the scene. In the present study, we focused on the analysis of EMS-witnessed cases with access to information on the initial SCA rhythm.

Importantly, we were able to replicate our findings in a geographically distinct SCA cohort from Ventura, CA, which mitigates the possibility of overfitting or systematic biases. Given the significant differences in demographics and clinical characteristics between Oregon SUDS and Ventura PRESTO, our findings suggest that the AI model may generalize well in external data sets with distinct patient profiles. Moreover, the AI model retained similar performance in the external dataset despite a significantly different distribution of PEA and VF in comparison to the training data set.

In comparison to previously used conventional statistical methods, the AI model identified novel determinants

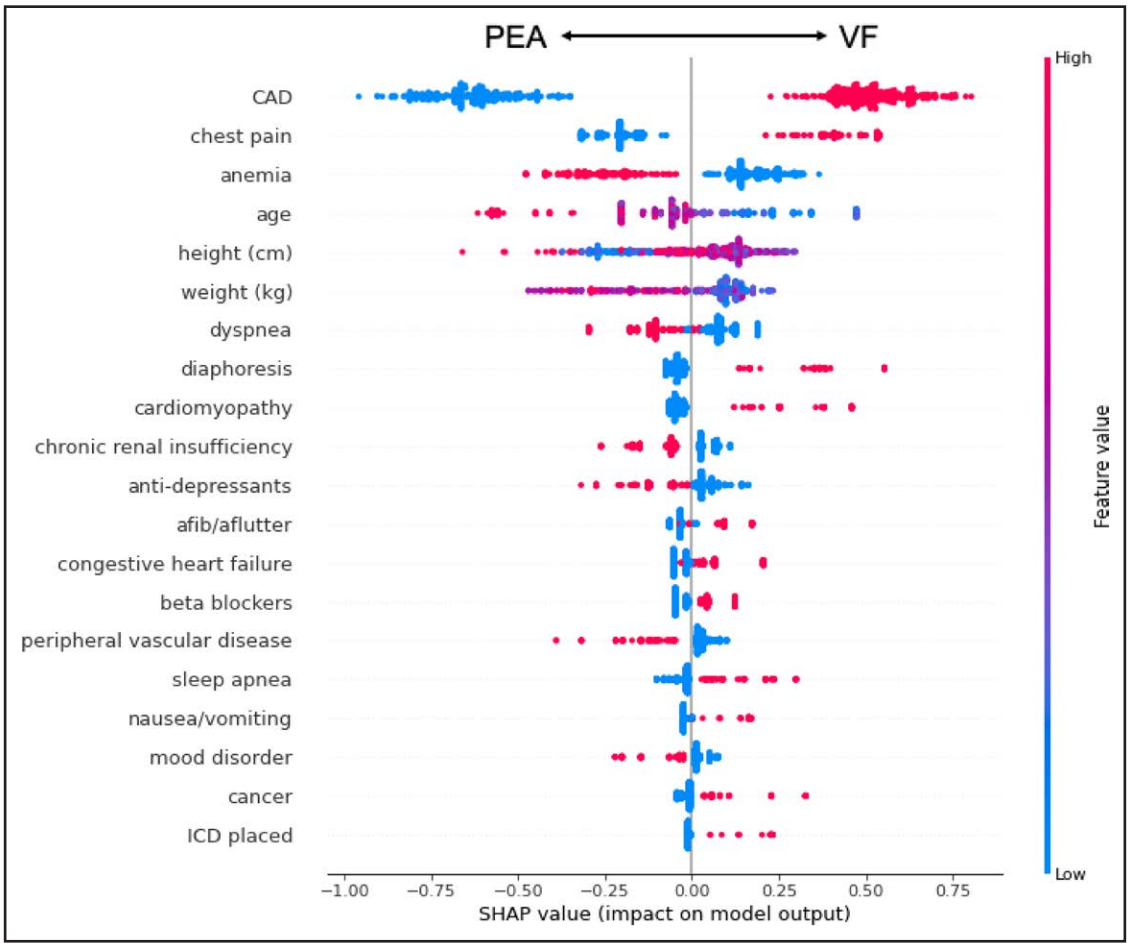

Figure 3. Shapley additive explanations (SHAP) values for all patients.
SHAP values show the importance of each feature for the artificial intelligence model in the identification of pulseless electric activity (PEA) and ventricular fibrillation (VF). SHAP values are calculated for each patient, and 1 data point represents 1 sudden cardiac arrest (SCA) case. In this figure, data points are mixed from the internal and external cohort SCA cases. Afib indicates atrial fibrillation; Aflutter, atrial flutter; CAD, coronary artery disease; and ICD, implantable cardioverter defibrillator.

of initial rhythms, that is, anemia, weight, height, and chronic kidney disease. Our results are consistent with findings from the Fingesture study, in which underlying CAD and ischemic cardiomyopathy were important determinants of VF.[23] A higher prevalence of preexisting CAD likely explains the importance of chest pain in predicting VF. Prior reports on EMS-witnessed out-of-hospital SCA cases from the OPALS study and the VACAR registry have also demonstrated that prearrest chest pain predicts VF while prearrest dyspnea predicts nonshockable rhythm.[24,25] However, these studies did not use AI techniques to identify key determinants of initial SCA rhythm.

Although the relationship between CAD/chest pain and VF has been previously recognized, other SCA rhythm determinants in our study represent novel findings. Notably, anemia had a strong association with PEA. One possible reason is that anemia predisposes to hypoxemia—a common precipitator of PEA. On the contrary, PEA is a more common presenting rhythm in elderly and sick patients,[11] and anemia is often related to a high comorbidity burden and may thus represent a sign of poor overall health. This contention is supported by the finding that older age and chronic kidney disease were also determinants of PEA in our study.

Another PEA determinant identified in our study was higher body weight, which in SCA cases is likely related to obesity.[26,27] While this is a novel finding, prior studies have indirectly associated obesity-related SCA and nonshockable rhythms because both are more likely to occur at night.[28–30] One possible explanation is obesity-related obstructive sleep apnea, which predisposes to nighttime bradyarrhythmias which in turn are a potential trigger for PEA.[31,32] In contrast to body weight, higher height was a determinant of VF. In this context, it is interesting to note the previously established association between greater height and increased risk of atrial fibrillation.[33]

The progressively declining rate of SCA presenting as VF in recent decades has been reported from several international registries.[6–8] The progressively aging population, decreasing age-adjusted CAD mortality, and

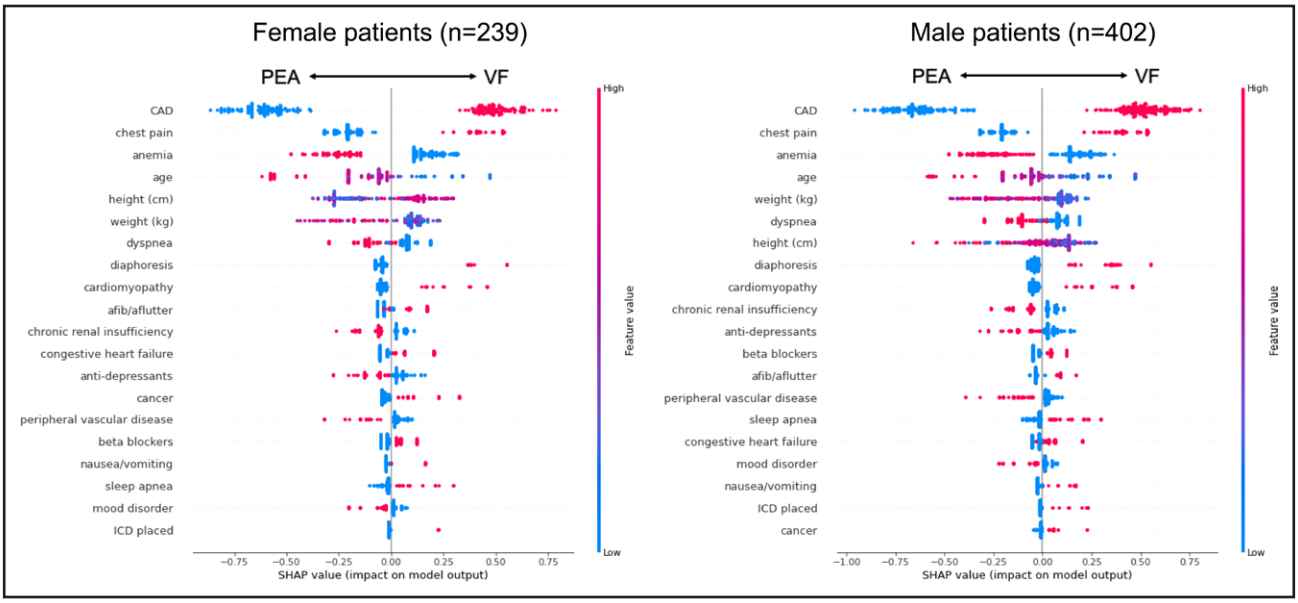

Figure 4. Shapley additive Explanations (SHAP) values for female and male patients.
SHAP values show the importance of each feature for the artificial intelligence model in the identification of pulseless electric activity (PEA) and ventricular fibrillation (VF). SHAP values are calculated for each patient, and 1 data point represents 1 sudden cardiac arrest (SCA) case. In this figure, data points are mixed from the internal and external cohort SCA cases. Afib indicates atrial fibrillation; Aflutter, atrial flutter; CAD, coronary artery disease; and ICD, implantable cardioverter defibrillator.

improvements in cardiovascular disease management (especially increasing usage of β-blockers and implantable cardioverter defibrillator) have been thought to contribute to this shift. β-Blockers have negative chronotropic and inotropic effects, and could suppress VF, resulting in an increased proportion of nonshockable SCA.[10] While our findings reinforce the role of increasing age and decreasing CAD mortality, these results do not support the contribution of β-blockers as an explanation for increased SCA presentation with PEA. Instead, use of β-blockers was a determinant of VF, while the use of antidepressants predicted PEA over VF, which is consistent with the prior literature.[34,35] Antipsychotics also have negative inotropic effects, and they have been associated with PEA,[34,35] but antipsychotic use was not an important feature in this analysis. Similarly, female sex and pulmonary diseases have been associated with PEA,[11] but in our study, these factors were not important for the model. Such differences between conventional and AI approaches may stem from the limitations of conventional methods to identify complex and nonlinear relationships.

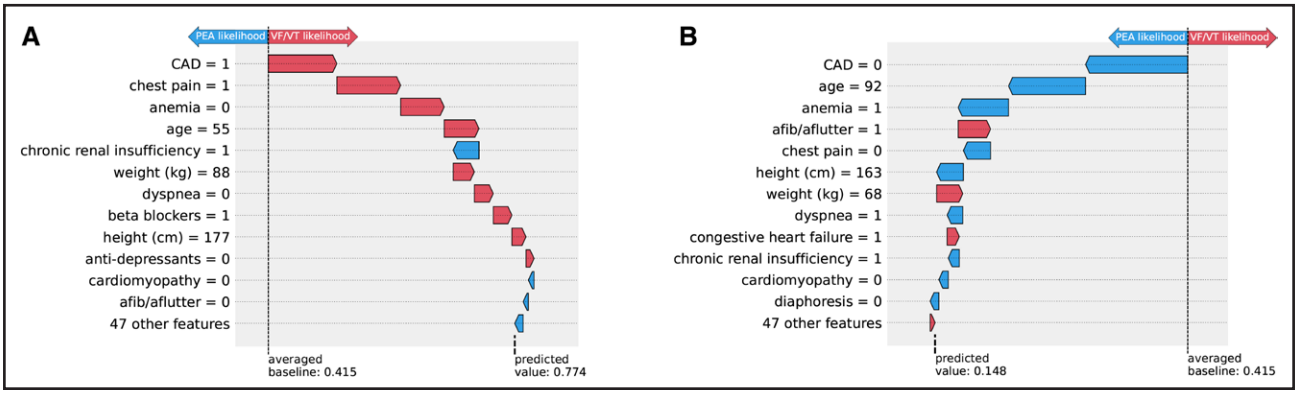

Figure 5. Representative examples of clinical features in two individual patients, one presenting with ventricular fibrillation and the other with pulseless electrical activity.
Examples of waterfall plots for a ventricular fibrillation (VF) case (**A**) and a pulseless electric activity (PEA) case (**B**) from the external cohort. The expected value is the average score for all patients in the internal cohort, where an optimal threshold is determined. The waterfall plot starts from the expected value and each row represents how the importance of each feature affects the model's prediction. For example, the VF case (**A**) had a history of CAD, pre-sudden cardiac arrest (SCA) chest pain, no history of anemia, and young age (55 y), which had the biggest impact on the model's prediction. The pulseless electric activity (PEA) case (**B**) had no history of coronary artery disease (CAD), older age (92 y), and a history of anemia which had the biggest impact on the model's prediction. Afib indicates atrial fibrillation; and Aflutter, atrial flutter.

Although the machine learning model achieved moderate accuracy, the AUC was comparable to common prediction models utilized regularly in current clinical practice, such as left ventricle ejection fraction in SCD prediction (AUC, 0.59–0.68)[36] or CHA2DS2VASc score in stroke prediction (AUC, 0.63–0.69).[37] Potential reasons for the moderate performance of the AI model may include our inability to capture input data regarding prearrest dynamic alterations in the cardiovascular system, as well as random events that may have an important contribution to SCA presentation (eg, acute MI, bradyarrhythmia). Although long-term SCA risk assessment has long been based on the measurements of moment statistics (eg, left ventricle ejection fraction), SCA is not, however, a fully deterministic event. Instead, the development of SCA may require triggering events that can induce life-threatening arrhythmias in vulnerable patients.[38] A variety of triggers and preceding dynamic cardiovascular alterations are likely to contribute to the presentation of SCA. Given that there are currently no specific treatment options for PEA, these novel findings have the potential to improve the current understanding of mechanistic differences between PEA and VF[36] (Figure 6).

Limitations

Although Oregon SUDS and Ventura PRESTO are designed to collect all out-of-hospital SCA cases prospectively, the data on prearrest clinical characteristics were obtained retrospectively. Hence, we were not able to collect comprehensive data for all variables (eg, ECG, echocardiography), leading to missing values and potentially unidentified rhythm determinants. By removing variables with >20% missingness in the internal cohort from the set of parameters to be used and imputed, we avoided most missing-data bias. However, we recognize that we cannot exclude bias from use of simple imputation methods and smaller extent of missingness in the remaining variables. Some dynamic risk factors preceding the SCA event may have an important contribution to the initial rhythm. However, given the unpredicted and sudden nature of SCA, collection of such data is extremely difficult.

Conclusions

An AI model could distinguish EMS-witnessed SCA cases presenting with PEA versus VF and was successfully validated in an external cohort. The model identified novel determinants of PEA and VF: previously diagnosed anemia, older age, high weight, and prearrest dyspnea were the most important determinants of PEA, while previously diagnosed CAD, prearrest chest pain, and young age were the most important determinants of VF. These findings could improve the mechanistic understanding of PEA and VF and may help to predict which individuals at increased risk of SCA will present with PEA versus VF.

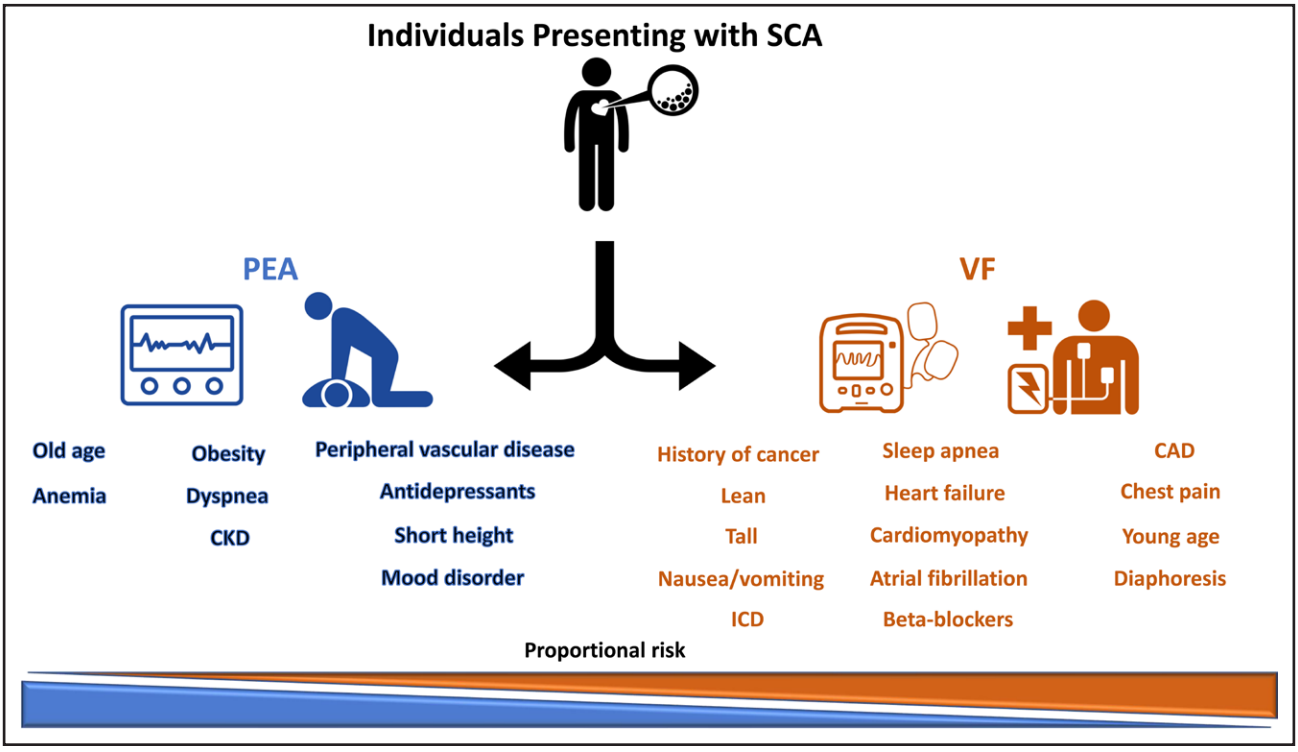

Figure 6. Schematic illustration of the key determinants of pulseless electric activity (PEA)-sudden cardiac arrest (SCA) and ventricular fibrillation (VF)-SCA.
CAD indicates coronary artery disease; CKD, chronic kidney disease; and ICD, implantable cardioverter defibrillator.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Tables S1–S4
Figures S1–S3

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