A Method to Predict Ventricular Fibrillation Shock Outcome during Chest Compressions

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Abstract

Background: Out-of-hospital ventricular fibrillation (VF) cardiac arrest is a leading cause of death. Quantitative analysis of the VF electrocardiogram (ECG) can predict patient outcomes and could potentially enable a patient-specific, guided approach to resuscitation. However, VF analysis during resuscitation is confounded by cardiopulmonary resuscitation (CPR) artifact in the ECG, challenging continuous application to guide therapy throughout resuscitation. We therefore sought to design a method to predict VF shock outcomes during CPR.

Methods: Study data included 4577 5-second VF segments collected during and without CPR prior to defibrillation attempts in N=1151 arrest patients. Using training data (460 patients), an algorithm was designed to predict the VF shock outcomes of defibrillation success (return of organized ventricular rhythm) and functional survival (Cerebral Performance Category 1–2). The algorithm was designed with variable-frequency notch filters to reduce CPR artifact in the ECG based on real-time chest compression rate. Ten ECG features and three dichotomous patient characteristics were then developed to predict outcomes. These variables were combined using support vector machines and logistic regression. Algorithm performance was evaluated by area under the receiver operating characteristic curve (AUC) to predict outcomes in validation data (691 patients).

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Results: AUC (95% Confidence Interval) for predicting defibrillation success was 0.74 (0.71–0.77) during CPR and 0.77 (0.74–0.79) without CPR. AUC for predicting functional survival was 0.75 (0.72–0.78) during CPR and 0.76 (0.74–0.79) without CPR.

Conclusion: A novel algorithm predicted defibrillation success and functional survival during ongoing CPR following VF arrest, providing a potential proof-of-concept towards real-time guidance of resuscitation therapy.

Introduction

Out-of-hospital cardiac arrest (OHCA) results in over 300,000 deaths each year in the United States.[1] OHCA is commonly caused by ventricular fibrillation (VF), an electrically-disorganized ventricular arrhythmia which causes ineffective mechanical contraction and circulatory collapse.[1,2] Current treatment protocol for VF OHCA includes high-quality cardiopulmonary resuscitation (CPR) briefly interrupted every two minutes for rhythm analysis and defibrillation shock but otherwise performed continuously until return of spontaneous circulation.[3,4] Overall survival from witnessed VF OHCA is approximately 30%, though there is a nearly ten-fold variability in survival across regional emergency medical services systems.[5,6] This range in outcomes suggest that VF OHCA is a potentially modifiable condition for which modifications to current protocols may be beneficial and merit exploration.

Observational studies have indicated that VF OHCA is a heterogeneous and dynamic entity, suggesting that the current uniform treatment approach may not optimally target case-specific physiology.[2,7–9] VF resuscitation may instead benefit from a targeted strategy that delivers selected medication, defibrillation, and CPR with dosage, sequence, and timing tailored to the individual patient.[10–13] A challenge to such a strategy is accurate real-time assessment of patient status to guide their immediate treatment. However, there is now increasing evidence that real-time myocardial physiology during VF can be assessed using the electrocardiogram (ECG).[14,15] Specifically, VF ECG characteristics have been shown to predict the likelihood that a defibrillation shock will produce the near-term outcome of an organized rhythm and even the long-term clinical outcome of survival.[16–19] The application of such information to inform a patient-specific profile of medication, shock, and CPR care could dramatically alter our current 'one-size-fits-all' approach to resuscitation and its consequent outcome.

During active resuscitation, chest compression artifact during CPR obscures the ECG signal and can confound ECG analysis.[20–22] CPR would therefore need to be interrupted to allow accurate real-time estimation of physiologic status using VF ECG characteristics, but even brief CPR interruption undermines forward blood flow and reduces the likelihood of successful resuscitation.[23,24] Ideally, the ECG would be assessed continuously during CPR and used to inform time-sensitive treatment choices throughout resuscitation.[25,26]

Such a strategy could potentially enable real-time titration of CPR and medication based on a patient's status, advancing an approach for VF treatment whereby CPR is interrupted only once a shock is likely to produce organized rhythm and survival.

Therefore, in the current investigation we sought to develop an algorithm to predict the short- and long-term outcomes of VF shock without requiring CPR interruption. The proposed algorithm could potentially provide the basis to inform patient-specific VF treatment decisions during resuscitation while supporting the best practice of high-quality continuous CPR.

Methods

Data

Study Design, Population, and Setting—The investigation was a cohort study of out-of-hospital cardiac arrests presenting to emergency medical services (EMS) with an initial rhythm of VF from 2005–2015 in King County, WA (excluding Seattle) that had complete defibrillator recordings. The cohort included patients treated with Lifepak 12, Lifepak 15 (Physio-Control, Redmond, WA), HeartStart FR3, and HeartStart MRx (Philips Healthcare, Bothell, WA) biphasic defibrillators. Patients were excluded if they were treated by a public access or police defibrillator prior to EMS arrival or were <18 years in age.

In accordance with applicable regulations, the Research Review Committee of King County Public Health and the Institutional Review Board at the University of Washington Human Subjects Division approved the study and waiver of informed consent.

Data Resource—The study system maintains a clinical registry that uses data resources including the dispatch recording, EMS written reports, hospital records, death certificates, and the defibrillator recording. These data sources are systematically abstracted to determine OHCA circumstances, patient demographics, prehospital care, and clinical outcomes. The registry is organized according to the Utstein template.[27]

Study Outcomes—We evaluated both short- and long-term patient outcomes. Short-term outcome was defibrillation success, defined as the return of an organized rhythm with distinct QRS complexes at a rate of >12 per minute after a defibrillation attempt (Figure 1). Successful long-term outcome was survival with functional neurologic status, defined as survival to hospital discharge with a Cerebral Performance Category of 1 or 2.[28]

ECG Data—We sought to combine clinical and ECG characteristics to achieve prediction of patient outcomes. When available in continuous defibrillator recordings, we collected one 5-s VF ECG segment during chest compressions followed by an adjacent 5-s segment without compressions prior to a shock (Figure 1). ECG segments were collected concurrently with transthoracic impedance (TTI) to confirm CPR status.[29] ECG data were collected at sampling rates ranging from 125 – 250 Hz and TTI data were collected at rates ranging from 61 – 200 Hz. All signals sampled at rates lower than 250 Hz were resampled to 250 Hz (Supplementary Material A). Data and signal processing were performed with MATLAB 2018 (MathWorks, Natick, MA) and RStudio 1.1 (RStudio, Boston, MA).

Algorithm Description

An overview of the proposed algorithm is shown in Figure 2.

ECG Filtering—During CPR, chest compression artifact in the ECG is generally concentrated near a fundamental frequency of approximately 2 Hz but can produce transient and harmonic artifacts up to 20 Hz.[20,30] Since VF commonly has a dominant frequency between 3–8 Hz which may overlap compression harmonic frequencies, ECG filtering to reduce chest compression artifact may also attenuate essential VF frequency content.[31] Therefore, in the current algorithm, filtered and unfiltered ECG signals were analyzed in parallel to take potential advantage of artifact reduction in filtered data as well as increased VF content in unfiltered data.

To apply filtering, ECGs were first bandpass-filtered using a 1–30 Hz 4th-order Butterworth filter to reduce drift, ventilation artifact, and high-frequency transient and power noise. If chest compressions were automatically detected in the corresponding TTI signal using a previously-validated compression detection method [29], the bandpass-filtered ECG was also processed with a variable-frequency notch filter to reduce CPR artifact. We designed the notch filter with a series of three 2nd-order Butterworth band-stop filters to reduce the fundamental and first two harmonic compression frequencies based on the real-time estimated chest compression rate (Figure 3, Supplementary Material A). All filters were applied with a forwards-backwards implementation for linear phase.

ECG Features—Prior studies have proposed quantitative measures of the VF ECG to assess myocardial metabolism and predict patient outcomes.[14,32] These measures quantify features such as VF amplitude and frequency.[32–38] However, such features are designed to analyze ECGs without CPR, and are thus confounded by chest compression artifact.[25,39] Prior investigation has also suggested that combinations of multiple features may improve prognostic performance versus using a single feature.[39,40]

We therefore designed ten novel features of the VF ECG to quantify characteristics associated with prognosis while remaining robust against potential chest compression artifact (Figure 4). Two features per domain were included from domains previously demonstrated to predict outcomes: ECG amplitude [33], entropy [41,42], scalogram energy [32,43], dominant frequency [34,35,44], and Fourier spectrum characteristics [45]. Features were each empirically designed with variable parameters to allow optimization for use during chest compressions, and were only retained if their performance on training data was significantly predictive of survival.

Specifically, to quantify ECG amplitude while remaining robust against low-frequency artifact and intermittent transient noise, *Sliding Deviation* and *Sliding Peak* were defined as the median of the absolute standard deviation and peak amplitudes, respectively, within variable-length time windows (Supplementary Material B). To quantify the entropy in the ECG scalogram while mitigating the effects of CPR artifact, *Interfrequency Entropy* and *High-Frequency Entropy* (Supplementary Material C) were defined as the median Shannon entropies of specific scalogram frequency bands. To describe the energy in the ECG scalogram while reducing confounding by CPR, the *Shannon Energy* and

Interfrequency Shannon Energy (Supplementary Material C) were defined as the median of Shannon-transformed magnitudes at each frequency band and at each time step in the scalogram, respectively, within variable frequency limits. To represent the dominant ventricular fibrillation frequency, *Mean Maxima* was defined as the average dominant scalogram frequency within variable frequency limits, while *Maxima Fraction* was defined as the proportion of time the dominant scalogram frequency exceeds a frequency threshold indicative of good prognosis (Supplementary Material D). Finally, as a measure of spectral variation and self-similarity in the short-time Fourier transform, the *Short-Term Deviation* was defined as the median of standard deviations at each time step, while *Correlation Component* was calculated using principal component analysis of correlations between frequency bands (Supplementary Material E).

Support Vector Machine—We used support vector machine classifiers to combine individual ECG features into a single continuous output.[46,47] The classifiers were of the form $f(x) = \sum_{t=1}^{T} y_t \alpha_t K(x_{input}, x_t) + w_0$, where x_{input} is an N–dimensional input of ECG features, α_t are model parameters, w_0 is a constant, and T support vectors x_t with associated class assignments $y_t \in \{-1, 1\}$ are generated from training data. The selected gaussian kernel function $K(a, b) = \exp\left(-\gamma \sum_{j=1}^{N} (a_j - b_j)^2\right)$ represents similarity between arbitrary inputs a and b given kernel size γ. Support vector machine output values $f(x)$ were mapped to continuous probabilities using a sigmoid transformation of the form $\sigma(f(x)) = \left[1 + e^{A_0 f(x) + A_1}\right]^{-1}$ given trained parameters A_{0-1}.[48]

Dichotomous Patient Variables—We considered basic patient characteristics for use in the algorithm that would be available in a time-sensitive acute clinical setting.[49] Prior investigation has suggested a relationship between the interaction of age and sex with arrest outcome.[50,51] Therefore in the current investigation, we included the basic demographic characteristics of age (dichotomized at <60 years and denoted *Age*) and female sex (denoted *Sex*) as well as their interaction. Additionally, evidence indicates that short-term response to prior shock is associated with response to subsequent shocks.[9,52,53] Hence we also included whether the prior shock resulted in return of organized rhythm (denoted *Prior ROR*), when applicable. We assumed that automated inclusion of prior organized rhythm in a prognostic algorithm is feasible given recent advancements in rhythm classification during CPR.[26,54]

Logistic Model—We used logistic regression to generate a probability of good prognosis for each 5-s input segment (Figure 2). The logistic model incorporated the variables described above to predict outcome of VF shock, and was of the form:

$$P = \begin{cases} g(\beta_0 + \beta_1(SVM) + \beta_2(Age) + \beta_3(Sex) + \beta_4(Age \times Sex)) & \text{if } shock = 1 \\ g(\beta_0 + \beta_1(SVM) + \beta_2(Age) + \beta_3(Sex) + \beta_4(Age \times Sex) + \beta_5(Prior\ ROR)) & \text{otherwise} \end{cases}$$

where P represents the probability of successful outcome, the logistic function $g(z) = \frac{1}{1 + e^{-z}}$, *shock* represents the current shock cycle number, *SVM* is the output from

the support vector machine, *Age*, *Sex*, and *Prior ROR* are dichotomous patient characteristic variables, and β_{0-5} are the logistic model parameters.

Training of Features and Models—We used training data to develop and optimize the proposed algorithm (Figure 5). To optimize the ten novel ECG features for use on both filtered and unfiltered ECGs, we selected parameters (such as frequency limits and sliding window size) to maximize the area under the receiver operating characteristic curve (AUC) on training data for each feature. We then trained a support vector machine to combine all 20 ECG features calculated in parallel from filtered and unfiltered ECGs. Support vector machine kernel size and box constraint hyperparameters were selected by performing a grid search of 5-fold cross-validation error versus hyperparameter values on training data. In order to improve support vector machine generalizability, we intentionally underfit the parameters by allowing increased kernel size and reduced box constraint during grid search while maintaining a cross-validation error within an empirically-defined tolerance of the absolute minimum error (see Supplementary Material F).[39] The support vector machine output and dichotomous patient characteristics were combined to predict patient outcome using a logistic model which was trained using maximum likelihood estimation on the training data. Individual predictors for the logistic model were characterized by univariate odds ratios.

The algorithm was designed to operate during different CPR states (i.e. with and without chest compressions) and to predict multiple patient outcomes (i.e. defibrillation success and functional survival). Therefore, four versions of the algorithm were trained depending on CPR state and predicted outcome, each with a separate ECG feature parameter set, support vector machine model, and logistic model.

Algorithm Performance

We sought to assess the algorithm's prognostic performance and determine whether prediction of patient outcomes using the algorithm was greater versus leading VF prognostic methods described in prior investigations. For comparison against the current algorithm, we selected the best-performing method from a recent comprehensive benchmark of VF waveform measures, denoted the SVM24 method.[39] SVM24 was calculated as described in prior study as the support vector machine combination of 24 previously-described features of the ECG. For further comparison against the current algorithm, we also selected a method well-validated in literature, the Amplitude Spectrum Area (AMSA).[55] We selected a version of AMSA from recent study calculated as the frequency-weighted sum of discrete Fourier transform magnitudes from 1–26 Hz.[56]

Algorithm performance was characterized using validation data. We compared AUC values for prediction of short-term and long-term patient outcomes, both with and without CPR artifact, for the current algorithm versus SVM24 and AMSA using the DeLong method.[57] An alpha of 0.05 (adjusted for eight comparisons to 0.0063 using the Bonferroni correction) was used to determine the statistical significance of AUC differences. Confidence intervals for AUC values were calculated by stratified bootstrapping.

We sought to further illustrate potential of the proposed algorithm to monitor patient prognostic status and predict likelihood of positive outcomes in the presence of CPR artifact. Using validation data, we grouped the predicted outputs during chest compressions into four equally-spaced probability quartiles. To evaluate the algorithm's ability to stratify patients into these four different prognostic groups, we compared the predicted rates of positive outcome versus true rates of positive outcome within each probability quartile.

Results

The study cohort was comprised of 1151 patients divided randomly into 40% training (N=460) and 60% validation (N=691) groups (Table 1). There were 868 and 991 training ECG segments collected with and without chest compressions, respectively, and 1264 and 1454 validation ECG segments with and without chest compressions, respectively. There were more ECG segments collected without compressions primarily because in some cases there was not a full 5-s period of CPR between defibrillator electrode placement and initial shock.

Of the individual predictors used in the logistic model, univariate odds ratios for SVM and $Prior\ ROR$ were significantly predictive of the short-term outcome of return of rhythm. Likewise, univariate odds ratios for SVM, $Prior\ ROR$, Age, and the interaction of Age and Sex were significantly predictive of the long-term outcome of functional survival (Table 2).

Without CPR, the algorithm predicted both short-term and long-term outcomes (Table 3, Figure 6). Compared to the prior published methods of AMSA and SVM24 without CPR on validation data, the algorithm achieved significantly greater prediction of the short-term outcome of return of rhythm: AUC was 0.77 for the current algorithm versus 0.74 for AMSA (p<0.001 for difference) and 0.75 for SVM24 (p=0.005 for difference). The algorithm also achieved significantly greater prediction of the long-term outcome of functional survival versus AMSA but not SVM24: AUC was 0.76 for the current algorithm versus 0.74 for AMSA (p<0.001 for difference) and 0.75 for SVM24 (p=0.21 for difference).

The algorithm also predicted outcomes in the presence of CPR artifact (Table 3, Figure 6). Compared to AMSA and SVM24 during CPR on validation data, the algorithm achieved significantly greater prediction of return of rhythm: AUC was 0.74 for the current algorithm versus 0.66 for AMSA (p<0.001 for difference) and 0.70 for SVM24 (p<0.001 for difference). The algorithm also achieved significantly greater prediction of functional survival versus AMSA but not SVM24: AUC was 0.75 for the current algorithm versus 0.70 for AMSA (p<0.001 for difference) and 0.75 for SVM24 (p=0.60 for difference).

During CPR, the true rates of successful outcomes were similar to those predicted by the algorithm (Figure 7). For example, the group of n=501 validation samples with low predicted probabilities of survival in the lowest quartile (0–0.25) had a true observed survival outcome rate within this range (0.18), and the group n=92 samples with predicted probabilities of survival within the highest quartile (0.75–1) had a true survival outcome rate within this range (0.82).

Discussion

Summary

In this retrospective cohort investigation of VF OHCA, a novel algorithm applied with and without ongoing CPR demonstrated improved prediction of the short-term outcome of defibrillation success compared to leading prior methods. Prediction of functional survival was also similar to the best-performing prior method. These results suggest that the current algorithm is an iterative step forward towards the goal of uninterrupted monitoring of patient physiologic status to enable a patient-specific approach to resuscitation.

Background

During VF, the myocardium is in a metabolically-demanding state concurrent with a complete interruption of coronary blood flow. These conditions rapidly deplete myocardial high-energy phosphate concentrations, reducing action potential conduction velocity and contractile function.[14,58,59] Successful restoration of organized rhythm following defibrillation therefore becomes increasingly unlikely as VF persists over time.[60–62] However, during resuscitation, sustained high-quality CPR can counteract the effects of prolonged VF and improve myocardial amenability to defibrillation by partially restoring coronary blood flow.[7,61,63] Therefore, rather than prioritizing early defibrillation, patients with a metabolically-compromised myocardium may instead benefit from a period of CPR to improve the myocardial substrate before a shock.[11,12] However, attempts to prioritize CPR using presumed myocardial status (e.g. based on EMS response time) have shown only a marginal survival benefit.[64] Instead there may be greater potential to improve VF OHCA survival by tailoring resuscitation therapy based on a direct assessment of patient physiology.

Measures of the VF ECG waveform predict defibrillation outcomes, are associated with myocardial metabolic substrate concentrations, and change dynamically to reflect patient response to alterations in treatment.[14,59,65–67] VF ECG waveform measures have thus been proposed as a means to provide real-time prioritization of shock versus CPR throughout resuscitation.[16–18] However, as with most ECG-based algorithms, these measures have been designed to analyze ECGs free of chest compression artifact.[20] This characteristic limits their application to few intermittent assessments that interrupt CPR, challenging the potential of such measures to continuously monitor patient status.[25] Indeed, recent prospective clinical investigation of a VF waveform measure applied during a singular CPR interruption prior to shock did not demonstrate a significant benefit to survival. [67] Ideally, prognostic evaluation would instead be performed continuously during CPR throughout resuscitation. Such uninterrupted evaluation could provide a continuous measure of patient myocardial status and trajectory during VF, potentially enabling real-time titration of CPR and medication to achieve the best possible defibrillation outcome.[10,25]

Algorithm Performance

We therefore sought to design an algorithm to predict patient outcomes both during and without CPR, and to determine whether performance was improved compared to leading prior predictive methods. In recent investigation, we conducted a benchmark of existing

VF prognostic methods during CPR and identified a best-performing method (termed the SVM24) among the 27 previously-published approaches tested.[39] When compared to the SVM24 method, the current algorithm exhibited significantly-improved prediction of defibrillation success. However, performance for predicting functional survival was only marginally improved versus SVM24.

We also compared the current algorithm to a classical method – the AMSA – which has been well-validated in retrospective human studies and is currently undergoing prospective investigation for clinical application.[55,56,68,69] Compared to AMSA, the current study algorithm demonstrated a significant AUC increase on validation data both with and without CPR.

Algorithm Design

We hypothesize that the observed performance of the current algorithm was enabled primarily through three attributes which distinguish it from the SVM24 and AMSA methods: Parallel use of filtered and unfiltered ECGs, design and combination of ECG features, and inclusion of dichotomous patient characteristics.

First, the algorithm analyzed filtered and unfiltered ECGs in parallel. ECG filtering improved amplitude-based features susceptible to ECG fluctuations caused by chest compression artifact and high-frequency noise, such as the *Sliding Peak* feature. On the other hand, use of unfiltered ECG data was generally more suitable for time-frequency features, such as the *Shannon Energy* feature. During CPR, such time-frequency features may not require notch filtering at estimated compression frequencies due to an inherent ability to ignore lower-frequency CPR artifact using variable frequency cutoffs, and may also utilize high-frequency VF content indicative of good prognosis that might otherwise be attenuated by bandpass filtering.

Second, ECG features were designed to quantify multiple prognostic qualities of the VF waveform related to myocardial metabolic status, such as amplitude, entropy, high-frequency energy, and dominant frequency.[32–38,46,47] This collection of ECG features was then combined using machine learning models trained to predict different resuscitation outcomes during each CPR state. We hypothesize that separately training models to predict specific outcomes during specific CPR states enabled improved performance over use of a single model for all conditions, since different VF waveform features are affected differently by CPR artifact and may also differ in their indication of specific resuscitation outcomes. [22,62] For instance, with regards to the effects of CPR, VF energy as described by the *Interfrequency Shannon Energy* feature was most predictive during CPR when calculated from frequencies above 13 Hz (hence avoiding most lower-frequency compression artifact), but was most predictive without CPR when calculated from frequencies above 5 Hz (thus including increased VF frequency content). As another example with regards to specific resuscitation outcome, the amplitude-based feature *Sliding Deviation* was generally most predictive of defibrillation success, whereas the time-frequency feature *Interfrequency Shannon Energy* was generally most predictive of functional survival (Supplementary Material G). Thus, use of separately-trained features and models to predict different resuscitation outcomes during both CPR states may enable simultaneous prediction of

different outcomes, even in cases with disparate prognoses (e.g. positive short-term prognosis but negative long-term prognosis, such as in Figure 6c–d).

Third, use of dichotomized variables such as *Prior ROR* improved prognostic performance over that of the ECG alone, with an observed validation AUC increase (versus ECG-only prediction) ranging from 0.01–0.04 overall depending on the predicted outcome (Supplementary Material G). Consistent with prior investigations, we observed a significant improvement in prognostic prediction by including response to prior shocks, and only a marginal improvement by including patient demographic variables.[50,52,53]

Clinical Implications

The current algorithm demonstrates potential to estimate probability of successful outcomes during CPR. These prognostic probabilities could potentially be used to monitor patient status and observe real-time effects from CPR and medications on the myocardial substrate during resuscitation. For instance, a prognostic indicator corresponding to the current predicted probability quartile (e.g. Figure 7) could be displayed to rescuers to inform real-time treatment decisions, such as determining when CPR and vasopressor medications have improved shock-resistant myocardium enough to enable successful defibrillation.[25] Therefore while prospective clinical investigation is required to determine how the current algorithm might actually be applied in practice, the results of the present study suggest potential to improve the current one-size-fits-all protocol for OHCA resuscitation by enabling a more patient-specific approach.

Limitations

The investigation used data collected from four different device models with unique hardware-based filtering bandwidths and sampling rates, which may reduce overall AUC for prognostic analysis when analyzed uniformly across devices.[39] However, the current results highlight the cross-platform applicability of the algorithm. While the algorithm outperformed prior methods, overall AUC was not optimal, hence the algorithm's utility in clinical practice is uncertain. The algorithm incorporated dichotomous patient variables presumed available to rescuers, and would thus require rescuer input to evaluate prognosis. However, a reduced version of the algorithm based solely on the ECG was also significantly predictive of outcomes (Supplementary Material H). The results of the current study were retrospective, and the potential for improved patient care using a prognostic algorithm is hypothetical. Prospective evaluation in a clinical setting would ultimately be required to determine whether a prognostic algorithm could improve patient survival.

Conclusion

A novel prognostic algorithm demonstrated a significant improvement in prediction of defibrillation success versus best-performing published methods regardless of ongoing CPR. These results may support a more tailored, patient-specific approach to resuscitation that could potentially direct treatment based on a patient's real-time prognostic status. Future investigation may seek to improve these prognostic methods by analyzing continuous ECG

data rather than isolated segments as in the current study, and by incorporating larger datasets to enable deep learning methods for development of improved ECG features.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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- Ventricular fibrillation measures predict cardiac arrest resuscitation outcomes

- Measures could be used to guide dosage and timing of resuscitation therapies

- During resuscitation, chest compressions reduce the accuracy of current measures

- We designed a method to predict resuscitation outcomes during chest compressions

- We observed improved prediction of defibrillation success versus current measures
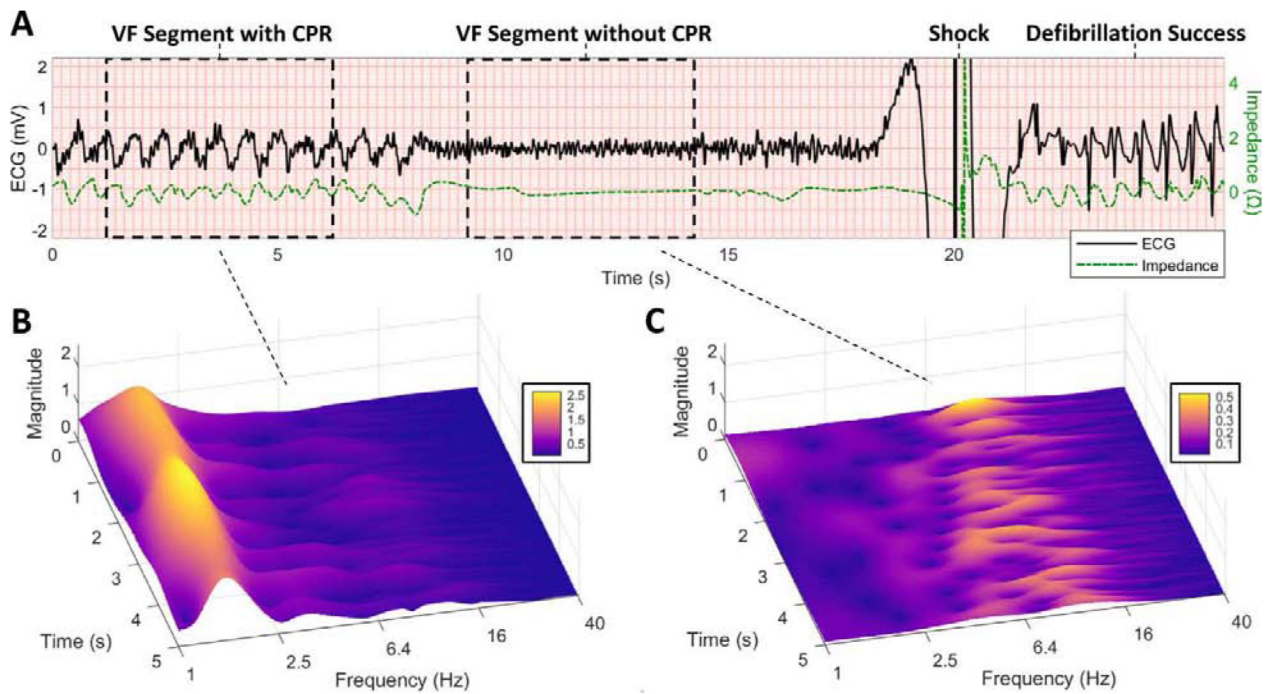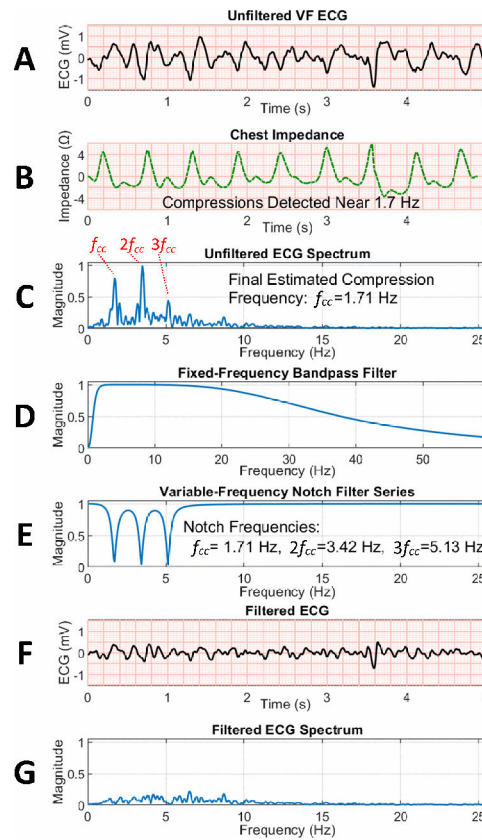
**Figure 1. Examples of VF Segment Collection with and without CPR**
(A) Example of adjacent 5-s VF ECG segments collected during CPR and without CPR prior to defibrillation shock. CPR is confirmed by chest compression oscillations in the concurrent impedance channel. Defibrillation success is confirmed by termination of VF and return of organized ventricular rhythm (QRS complexes) following shock. (B) Scalogram of VF during CPR illustrates dominant CPR fundamental at approximately 1.6 Hz with transient compression artifacts extending to higher frequencies. (C) Scalogram of VF without CPR illustrates a relatively high dominant VF frequency (ranging from approximately 6–12 Hz in this example), which may suggest an energetic myocardial metabolic substrate amenable to defibrillation. (CPR = cardiopulmonary resuscitation, ECG = electrocardiogram, VF = ventricular fibrillation.)

Figure 2. Algorithm Overview

The algorithm accepts a 5-s VF ECG input segment, a concurrent 5-s TTI input segment, and three dichotomous inputs. ECG features are calculated in parallel from filtered and unfiltered ECGs and incorporated with dichotomous variables to predict shock outcome. (CC = chest compressions, CPR = cardiopulmonary resuscitation, ECG = electrocardiogram, f_{cc} = chest compression frequency, SVM = support vector machine, TTI = transthoracic impedance.)

Figure 3. Filter Example

(A) Unfiltered VF ECG segment during chest compressions. (B) Compressions are detected in the concurrent transthoracic chest impedance signal. (C) Normalized spectrum of ECG during compressions, with compression fundamental and two harmonics visible. (D) 1–30 Hz bandpass filter. (E) Notch filter series based on estimated compression fundamental frequency f_{cc}. (F) Filtered ECG following bandpass and notch filtering. (G) Spectrum of filtered ECG confirms removal of the majority of compression fundamental and first two harmonics. (ECG = electrocardiogram, VF = ventricular fibrillation.)
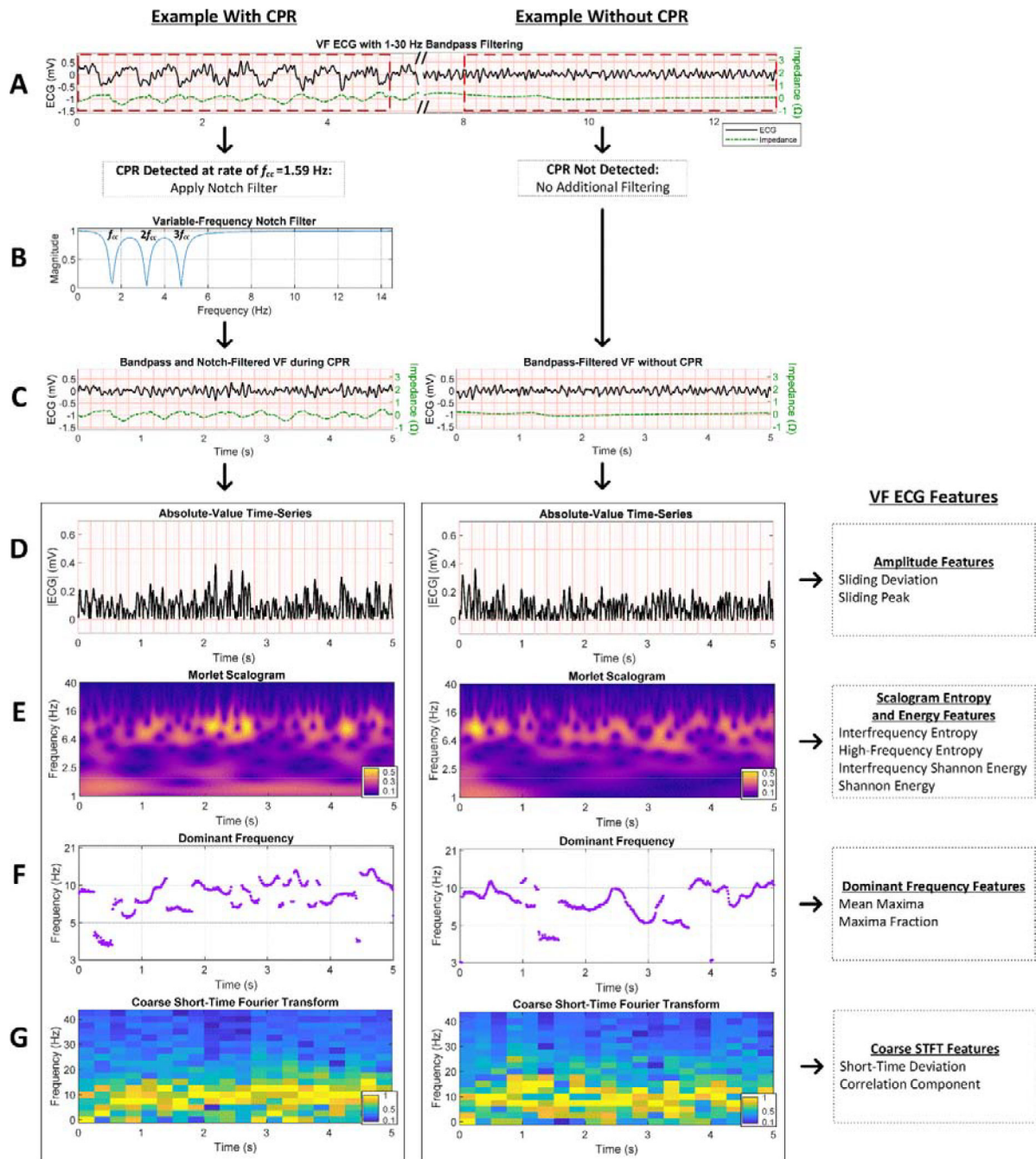
Figure 4. Examples of features from filtered ECGs with CPR versus without CPR
(A) Adjacent VF ECG segments after filtering with 1–30 Hz bandpass filter but prior to CPR detection and potential notch filtering. (B) When chest compressions are detected in the concurrent transthoracic impedance signal, a series of notch filters based on estimated compression rate f_{cc} are applied to the ECG to attenuate the compression fundamental and first two harmonic frequencies. (C) VF ECGs with CPR versus without CPR after filtering. (D) Amplitude features are calculated from the absolute time-series of the ECG. (E) Time-frequency features are calculated from the Morlet wavelet-based scalogram of the ECG. (F) Dominant frequency features are calculated from the frequencies of greatest

magnitude in the wavelet scalogram. (G) Coarse STFT features are calculated from the STFT of the ECG calculated using non-overlapping box windows. (CPR = cardiopulmonary resuscitation, ECG = electrocardiogram, STFT = short-time Fourier transform, VF = ventricular fibrillation.)
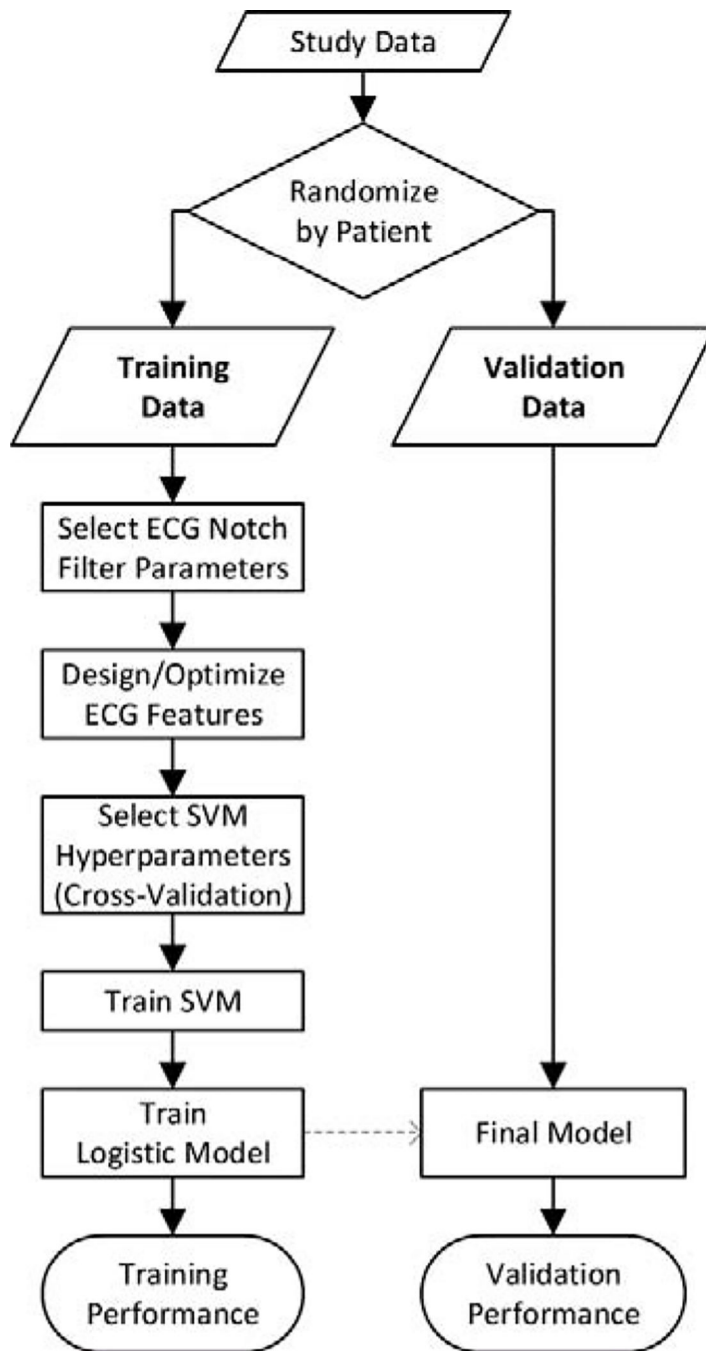
Figure 5: Training and Validation Procedure
The use of training and validation data for development and evaluation of the proposed
method is illustrated. (ECG = electrocardiogram, SVM = support vector machine)
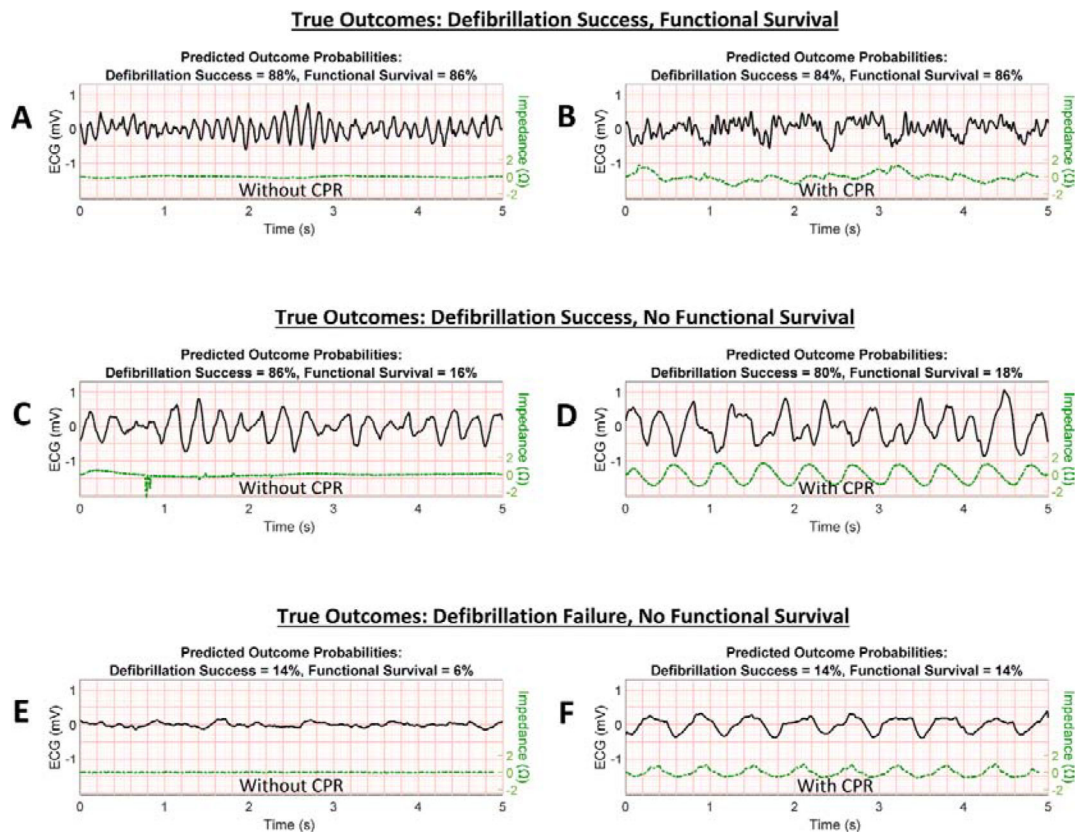
Figure 6. Specific examples of predicted outcomes versus true outcomes

Selected VF ECG validation segment examples from six patients are displayed with algorithm-predicted probabilities for defibrillation success (return of organized rhythm following shock) and functional survival (survival with Cerebral Performance Category of 1 or 2). VF examples with good prognosis (actual outcomes of successful defibrillation and functional survival) are shown without CPR (A) and during CPR (B). VF examples with mixed prognosis (actual outcomes of successful defibrillation but no functional survival) are shown in (C) without CPR and (D) during CPR. VF examples with poor prognosis (actual outcomes of unsuccessful defibrillation and no functional survival) are shown in (E) without CPR and (F) during CPR. (CPR = cardiopulmonary resuscitation, ECG = electrocardiogram, VF = ventricular fibrillation.)
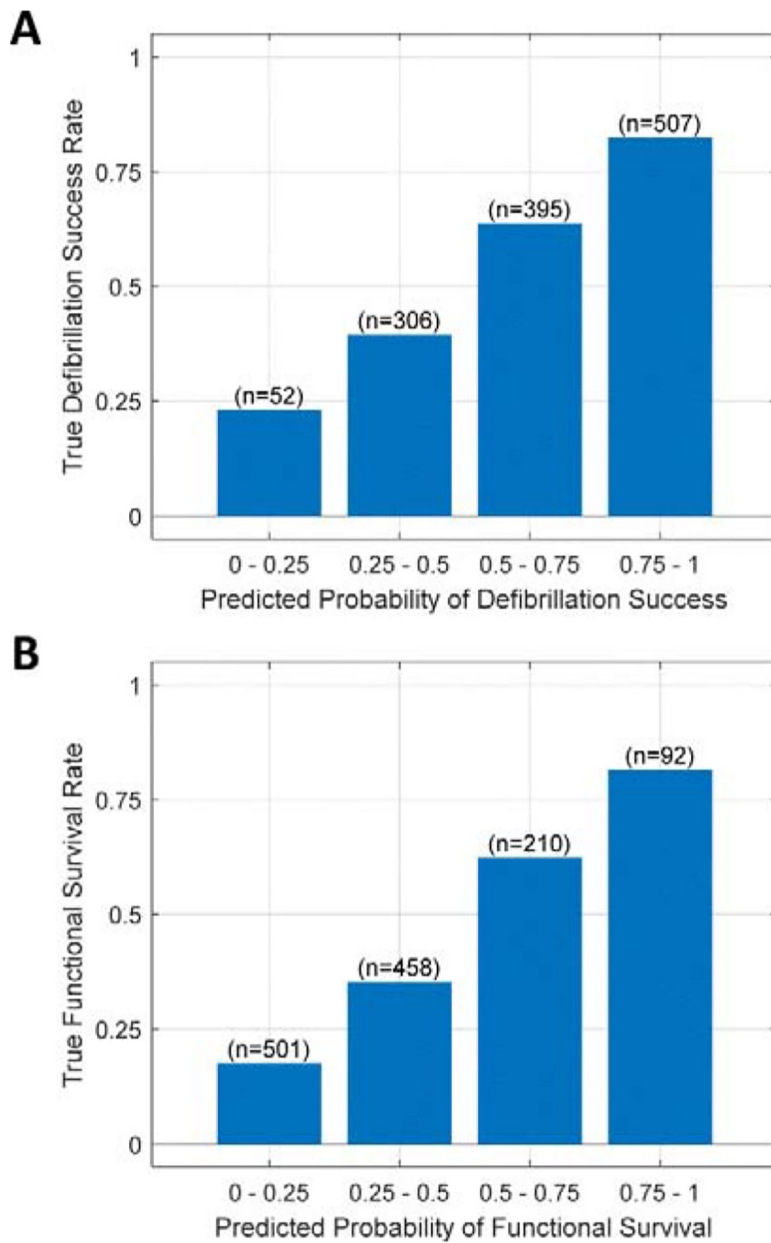
Figure 7. Predicted outcomes versus true outcomes

True rates of positive outcome are shown within each quartile of predicted probabilities of positive outcome, using validation data during CPR. (A) The true rates of defibrillation success were within the predicted probability quartiles for defibrillation success. (B) The true rates of functional survival were within to the predicted probability quartiles for functional survival. (n = number of validation segments within each predicted probability decile)

Table 1:

Patient characteristics

Patients, n	1151
Female, n(%)	265(23.0)
Age, median (IQR)	61(52, 72)
Cardiac etiology, n(%)	1080(93.8)
Location, n(%)	
Home	707(61.4)
Public	399(34.7)
Nursing Home	45(3.9)
Arrest before EMS arrival, n(%)	1093(95.0)
Witnessed, n(%)	885(76.9)
Bystander cardiopulmonary resuscitation, n(%)	833(72.4)
EMS Response (minutes), median (IQR)	5(4, 6)
Total shocks, median (IQR)	3(2, 6)
Return of spontaneous circulation at end of EMS care, n(%)	817(71.0)
Admit to hospital, n(%)	810(70.4)
Survive to hospital discharge, n(%)	524(45.5)
Survive with cerebral performance category 1 or 2, n(%)	471(40.9)

(EMS = emergency medical services, IQR = interquartile range)

Table 2:

Odds ratios for predictors in logistic model

Predictor	Odds Ratios for Defibrillation Success				Odds Ratios for Functional Survival			
	Training		Validation		Training		Validation	
	−CPR	+CPR	−CPR	+CPR	−CPR	+CPR	−CPR	+CPR
Age (<60)	1.0 (0.78–1.3)	0.86 (0.66–1.1)	1.1 (0.89–1.4)	1.1 (0.84–1.3)	1.7 (1.3–2.2) [*]	1.8 (1.4–2.2) [*]	1.8 (1.5–2.3) [*]	1.7 (1.4–2.2) [*]
Sex (Female)	1.2 (0.85–1.6)	1.3 (0.89–1.8)	1.3 (1.0–1.7)	1.3 (1.0–1.8)	1.0 (0.76–1.4)	1.2 (0.87–1.7)	1.1 (0.88–1.4)	1.0 (0.80–1.4)
Age × Sex	1.5 (0.9–1.4)	1.2 (0.75–2.0)	1.4 (1.0–2.0)	1.5 (1.0–2.2)	2.3 (1.5–3.6) [*]	2.5 (1.6–4.1) [*]	1.9 (1.4–2.7) [*]	1.8 (1.2–2.5)
Prior ROR	4.6 (3.2–6.6) [*]	4.2 (3.0–5.9) [*]	5.8 (4.2–4.9) [*]	5.5 (4.1–7.4) [*]	2.8 (2.0–4.1) [*]	2.3 (1.6–3.2) [*]	2.2 (1.7–3.0) [*]	2.3 (1.7–3.0) [*]
SVM	2.4 (2.0–2.7) [*]	2.2 (1.8–2.5) [*]	2.6 (2.3–3.0) [*]	2.1 (1.9–2.4) [*]	2.7 (2.3–3.1) [*]	2.3 (2.0–2.7) [*]	2.7 (2.4–3.1) [*]	2.7 (2.3–3.1) [*]

Univariate odds ratios (95% confidence interval) of successful outcome are presented for each predictor included in the final logistic regression model. Odds ratios for continuous variables are standardized. *Prior ROR* only includes segments prior to shocks 2–4. (−CPR = ECG segments without chest compressions, +CPR = ECG segments with chest compressions, Prior ROR = prior return of organized rhythm, SVM = support vector machine output).

[*] univariate odds significantly greater than 1 after Bonferroni correction (p<0.0012)

Table 3:

AUC values

	AUC for Predicting Defibrillation Success				AUC for Predicting Functional Survival			
	Training		Validation		Training		Validation	
	−CPR	+CPR	−CPR	+CPR	−CPR	+CPR	−CPR	+CPR
Study algorithm	0.76 (0.72–0.79)	0.74 (0.71–0.77)	0.77 (0.74–0.79)	0.74 (0.71–0.77)	0.78 (0.75–0.81)	0.75 (0.72–0.79)	0.76 (0.74–0.79)	0.75 (0.72–0.78)
SVM24 (Coult 2019) [39]	0.72 (0.69–0.75)	0.69 (0.65–0.72)	0.75 (0.72–0.77)	0.70 (0.67–0.73)	0.75 (0.72–0.78)	0.73 (0.70–0.77)	0.75 (0.73–0.78)	0.75 (0.72–0.78)
AMSA$_{1-26 Hz}$ (Firoozabadi 2013) [56]	0.71 (0.68–0.74)	0.66 (0.62–0.70)	0.74 (0.71–0.76)	0.66 (0.63–0.69)	0.74 (0.71–0.77)	0.70 (0.66–0.73)	0.74 (0.71–0.76)	0.70 (0.67–0.73)

AUC values (95% confidence interval) for prediction of patient outcomes are presented for training and validation datasets. (AMSA = amplitude spectrum area [56] method, AUC = area under the receiver operating characteristic curve, −CPR = ECG segments without chest compressions, +CPR = ECG segments with chest compressions, SVM24 = support vector machine combination of 24 previously-published features [39].)