Analysing the Dynamics of Pulseless Electrical Activity during Cardiopulmonary Resuscitation

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Abstract

Possible clinical states of a cardiac arrest patient are ventricular fibrillation/tachycardia (VF/VT), asystole (ASY) or pulseless electrical activity (PEA), and the treatment goals are return of spontaneous circulation (ROSC) and neurologically intact survival. Waveform analysis has been used in VF to predict treatment outcomes and we hypothesised that similar analysis in PEA could predict transformation to ROSC. We analysed 120 and 83 PEA segments prior to transitions to ROSC and ASY, respectively, to investigate the ability of ten electrocardiograph (ECG) features to predict transitions to ROSC or ASY using neural networks. The feature combination that yielded the best discrimination had a mean$\pm$SD area under the receiver operating characteristics curve of 0.88$\pm$0.02. The results suggest that the ECG contains information regarding the dynamics of PEA which can be used to study effects of therapies in cardiac arrest patients.

1. Introduction

The cardiac arrest state is unstable, and will alternate either spontaneously or due to intervention between ventricular fibrillation/tachycardia (VF/VT), asystole (ASY) and pulseless electrical activity (PEA). The goals of cardiac resuscitation are to generate return of spontaneous circulation (ROSC) in the short term, and neurologically intact survival in the long term.

PEA is frequent during therapy of cardiac arrest and has numerous electrical manifestations of which the two most important are *Pseudo PEA* and *True PEA*. True PEA is defined as the total absence of myocardial contraction. Pseudo PEA is characterised by weak myocardial contractions producing minimal aortic pressure and often has narrow QRS complexes and shorter RR intervals and a higher rate than true PEA. Pseudo PEA has also proven to be more amenable to therapy[1].

PEA is a common state during cardiac arrest either as the initial rhythm or occurring during resuscitation efforts. A large fraction of successfully resuscitated patients go through a stage with PEA at some point during the resuscitation process, and aggressive resuscitation attempts are required.

Waveform analysis reflecting the dynamics within PEA, e.g. characteristics which discriminate between true- and pseudo PEA, could add information on the patient response to therapy and be used to generate prognostic information similar to that gained from VF waveform analysis. Clinically, estimating changes in the probability of transition from PEA to ROSC could lead to prolonged and more aggressive/invasive efforts in cases with detected responsiveness to therapy and earlier termination of futile resuscitation.

Our hypothesis is that PEA changes dynamically due to time and interventions, so that in some cases it is more probable that a spontaneous change of state will result in ROSC than in ASY. We investigate if these changes can be characterised by features calculated from the PEA waveform.

2. Methods

We extracted ECG waveform segments to represent PEA with spontaneous transformations to alernative rhythms from 689 patients and categorised them according to resulting rhythm. The cardiac arrested patients were treated with a Heartstart 4000SP monitor/defibrillator (Laerdal Medical, Stavanger, Norway) from 2002 to 2005. These defibrillators were modified for expanded signal measurements. The patient data originated from ambulance services in Akershus (Norway), Stockholm (Swe-

den) and London (UK). In addition the data included patients treated in the acute care unit of the emergency department at the University Hospital in Vienna (Austria) and further patients with in-hospital cardiac arrest at the University of Chicago (USA). The medical experts at each site annotated the rhythm changes in the ECG. From this material we extracted all PEA segments not influenced by either chest compressions, defibrillation or degrading noise. The PEA segments of interest consisted of PEA rhythm prior to transitions to ASY or ROSC. The data is divided into two classes, labelled ω_{ASY} and ω_{ROSC} as listed in table1.

Class	*# PEA Blocks*	*Description*
$\omega_{\mathbf{ASY}}$	134	PEA transition to ASY
$\omega_{\mathbf{ROSC}}$	249	PEA transition to ROSC

Table 1. Distribution of PEA blocks

This gave us 249 and 134 PEA segments prior to transitions to ROSC and ASY respectively. Some examples of waveforms from these two classes are shown in figure 1.

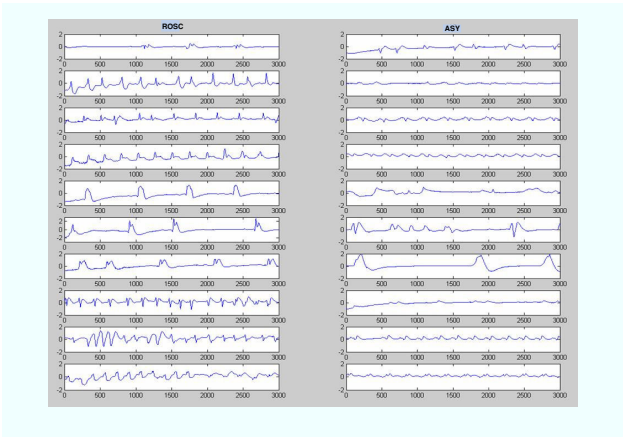

Figure 1. 20 randomly selected PEA segments prior to transition to ROSC (left) and ASY (right) with a duration of 6 *sec.*

In order to prevent suppression of PEA characteristics, the features were extracted from a rectangular sliding window of width 4s (2000 samples). P features are extracted from each window, k, to form feature vector $\mathbf{v}(k) = [v_1(k)\ v_2(k) \cdots v_P(k)]^T$ where $k \in [1, 2 \ldots, K]$. The windows overlap with 0.4 *sec.* It is ensured that the end of a segment is always represented. $\mathbf{v}$ is then calculated as the element-by-element median of all $\mathbf{v}(k)$. The median is used to suppress the influence of outliers in $\mathbf{v}(k)$. When extracting features for training purposes, PEA blocks are truncated to a signal length of 10s (5000 samples). The data 10s prior to onset of rhythm transition is kept, and the remaining is dumped.

Earlier analysis has presented promising results in discriminating between PEA and perfusing rhythm[2]. The following parameters were adapted from prior work and used in this study: average RR interval, number of detected QRS complexes, average QRS width, average QRS height, average ECG power, average ECG amplitude, average ECG amplitude exceeding 80% of maximum amplitude (MA80), angle, slope (average sample difference), signal length (SL) of the minimum phase correspondent (MPC), max MPC, form factor and the coefficient of a 6^{th} order polynomial fitting with additional fitting error[2, 3, 4, 5].

Neural networks were trained to discriminate between segments preceding ROSC and ASY in a 25 fold cross validation strategy. Receiver operating characteristics (ROC) curves were calculated and the the best performance was found according to the largest area under the curve (AUC) of the ROC graph.

In order to reduce the dimension of the feature vector, $\mathbf{v}$, and obtain a subset with suboptimal feature combinations a greedy search approach was applied. The greedy search evaluates a criterion function, J. Various functions may be used, but in our case the mean AUC of the classifier is used as criteria for the greedy search. The feature with the largest J among all P features in $\mathbf{v}$ is initially selected. In an iterative manner one by one feature is added to the subset according to the feature that yields the largest increase in J. The greedy search stops when no local improvement is possible.

In general the labelled samples D are randomly divided into two equally sized parts. One training set and one testing set. But, when dealing with limited data sets, training can be troublesome if not impossible due to the classifier's lack of generality. By applying cross validation techniques the generality of the classifier can be improved considerably. M-fold cross validation is a widely used method[6]. The training set was randomly divided into m disjoint sets of equal size n/m, where n is the total number of patterns in D. The classifier was trained m-times, each time with a different validation set. The estimated performance is the mean AUC of m-validations.

The performance of the classifier was evaluated in terms of sensitivity (probability of true positive prediction of ω_{ROSC}) and specificity (probability of true positive prediction of ω_{ASY}).and After varying sensitivity over specificity, the area under the ROC curve was calculated for each test set. The estimate of the classifier's performance was then calculated as the mean of the AUC over all test sets, and gives a general measure of the classifier's performance for different parameter settings. The standard deviation was also calculated to get an impression of the generality of the classifier.

The generality of the classifier is governed by the neural network architecture. A great number of hidden neu-

rons and excessive use of training epochs result in close to 100% sensitivity and specificity. A large deviation of sensitivity in testing would indicate over-training. Neural networks were trained with all combinations of hidden neurons, $n_H = [2, 4, \ldots, 20]$ and epochs, $k_{epochs} = [10, 20, \ldots, 200]$.

Finally, for a given subset of features the optimal classifier was determined as the one yielding the smallest number of neurons and epochs that did not jeopardise the over-all performance of the classifier.

3. Results

The window length that gave the best over-all performance was 4s (2000 samples), and was therefore used in evaluating the performance of various neural network architectures. In order to sustain generality in the performance of the neural network, the lowest number of epochs and nodes that did not jeopardise the over-all performance was chosen. The parameters were thus set to 50 training epochs and 10 hidden nodes. The performance of each feature in discriminating between ω_{ROSC} and ω_{ASY} is presented in table 2 in terms of mean AUC (standard deviation). When these features were combined in a greedy search, the performance of the classifier was improved as shown in figure 2.

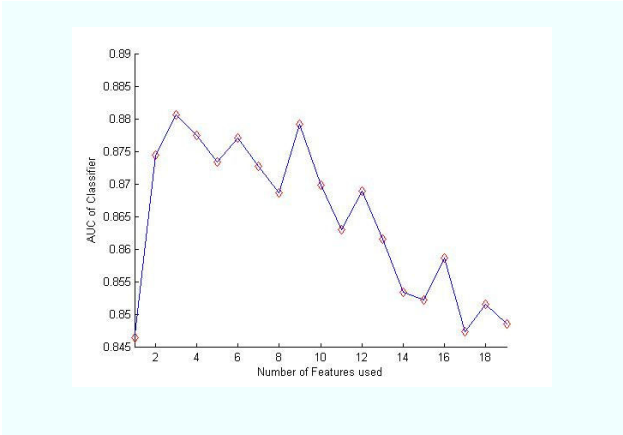

Figure 2. AUC as a function of feature dimension.

The feature combination that produced the best over-all performing classifier is presented in table 3, yielding a mean AUC±SD of 0.88±0.02.

4. Discussion and conclusions

The present results suggest that changes in PEA can be characterized quantitatively from the ECG waveform. As presented in table 3 it is shown that the selected features enable discrimination between PEA segments in change

v_{ECG}	Description	AUC
v_1	RR interval	0.58 (0.029)
v_2	Number of QRS complexes	0.53 (0.03)
v_3	Average width of QRS	0.72 (0.01)
v_4	Average height of QRS	0.74 (0.01)
v_5	Average ECG power	0.74 (0.05)
v_6	Average ECG amplitude	0.65 (0.02)
v_7	MA80	0.72 (0.00)
v_8	Angle	0.71 (0.01)
v_9	Slope	0.85 (0.01)
v_{10}	SL of MPC	0.58 (0.02)
v_{11}	Max absolute MPC	0.62 (0.01)
v_{12}	Form Factor	0.74 (0.01)
v_{13}	PolyCoeff_1	0.47 (0.02)
v_{14}	PolyCoeff_2	0.68 (0.02)
v_{15}	PolyCoeff_3	0.71 (0.02)
v_{16}	PolyCoeff_4	0.71 (0.02)
v_{17}	PolyCoeff_5	0.73 (0.01)
v_{18}	PolyCoeff_6	0.69 (0.02)
v_{19}	Average PolyFit Error	0.44 (0.06)

Table 2. The mean AUC (standard deviation) of each feature.

Feature set	Included features	AUC±SD
v_{ECG}	v_9, v_4, v_{12}	0.88±0.02

Table 3. The mean AUC of the classifier derived from the best feature combination

of state to ROSC and ASY respectively. The best performing classifier is based on feature vector, $v = [v_9\ v_4\ v_{12}]$. Feature v_9 was by far the best single performing feature, and yielded a larger value for PEA in transition to ROSC. Slope represents the steepness of the ECG changes, and thus can be a measure of more synchronistic depolarization of myocardial cells. The value of v_4 was generally larger in transition to ROSC than of ASY. The height of the QRS is usually thought to represent the muscle mass depolarizing synchronously in the lead vector. The classifier was not considerably improved by introducing additional features. Figure 2 shows several possible well performing feature combinations with various dimensions. It is promising that features independent of QRS detection such as v_9, v_{10}, and v_{12} perform so well, since erroneous QRS detections arise due to the variable QRS complexes of the PEA waveforms.

One weakness of the study is that only PEA segments with transitions to ROSC and ASY were isolated. A similar study should be performed with the additional transitions to VF and VT present in the dataset. In a preliminary experiment, a classifier discriminating between ω_{ROSC} and $\omega_{nonROSC}$ yielded a mean AUC±SD of 0.75±0.02. This indicates that the analysis also captures the dynamics of PEA with transitions to VF and VT, but that these cases

are somewhere in between the extreme cases of transitions to ROSC and ASY.

The greedy search algorithm is suboptimal and excludes a vast number of possible feature combinations, and there may exist unexplored feature combinations that outperform our selection.

By introducing sophisticated filtering techniques, the discriminating power of the features might be enhanced. The investigation of specific frequency bands, as done in former VF analysis, should also be addressed in future studies[7]. A light-weight QRS-detection algorithm was used, and it might have suppressed predictive power with respect to QRS characteristics, due to erroneous QRS detection. By applying an improved QRS-detection algorithm, performance might be added to the results of the present study. It is also important to note that cross validation techniques were used to enable training and testing on the same dataset. The classifier should have been tested on yet another dataset, not influenced by the design process.

Some earlier studies have reported findings on the significance of changes in PEA waveform characteristics. One study classified PEA waveform morphology into several groups, ranging from PEA waveforms with normal QRS width and isoelectric ST and P waves, to PEA waveforms beyond QRS, P and T wave recognition. Patients who were successfully resuscitated had ECG tracings classified as belonging to the groups with the most recognisable QRS, P and T waveforms. We speculate that these classifications represent progressive stages, which accounted for their predicted value with respect to outcomes or response to therapy [1]. Post defibrillation PEA collected from porcine experiments of cardiac arrest showed shorter QRS-interval and higher PEA-rate in the animals that eventually had ROSC[8].

The results show that the ECG contains information regarding the dynamics of PEA which can be used to study the effects of therapies in cardiac arrest patients.

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