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Abstract

In this study, we examine whether it is reliable to use all successive shocks from one patient for the development of an outcome predictor model to discriminate "Success" versus *"No success". Vector of predictors $\overrightarrow{v}$ are extracted from time and non-linear dynamics domains and a Gaussian Mixture Model-based bayesian classifier, with probability density estimated by the Expectation-Maximization algorithm, is applied in order to detect shocks with "Success" according to the probability $P(\overrightarrow{v}/Success)$. A cross-validation analysis is performed independently on 136 first shocks (Group1) and 382 second and later shocks (Group2). At 5 s post-shock, an Organized Rhythm (OR) is considered as "Success" and Ventricular Fibrillation (VF) is defined as "No success". A decrease in performance of discrimination of OR versus VF between Group1 and Group2 is observed with an Area Under the ROC Curve of 0.82 and 0.65, respectively. This corroborates the current hypothesis that within-patient correlation affects defibrillation outcome prediction accuracy.*

1. Introduction

Ventricular Fibrillation (VF) remains a most common arrhythmia in many instances of sudden cardiac death. Over the last few decades, techniques have been developed to analyze the surface electrocardiogram (ECG) associated with VF, in an attempt to obtain more information about the state of the myocardium and predict defibrillation outcome. There is no doubt that the duration of VF remains one of the principal determinants for the likelihood of successful defibrillation. For patient with witnessed cardiac arrest, rapid defibrillation is strongly recommended. When the duration of untreated VF exceeds 4 or 5 min., performing Cardiopulmonary Resuscitation (CPR) for 90 s or 3 min. is recommended before any defibrillation attempt [1, 2]. However, the exact duration of sudden onset VF is not always clear for rescuer, and therefore, there is a need for regarding the priority of intervention to be performed, namely immediate defibrillation or reperfusion by prior chest compressions. Thus far, several non-invasive predictors of successful defibrillation in VF waveform of ECG have been reported. These predictors can be generally categorized into time domain [3–9], frequency domain [10, 11] and non-linear dynamics domain [12–16] and are used alone or combined [17, 18]. Moreover most of the predictor models have been developed on large databases including all shocks of each patient. Nevertheless Gundersen *et al.* mentioned that within-patient correlation affects defibrillation outcome prediction accuracy [9, 19]. To our knowledge, since repeated shocks in one patient were considered as dependant events, only Lin *et al.* [15] have decided to collect for analysis just the initial ECG waveform before each first time defibrillation.

The objective of this study is to evaluate the influence of all successive shocks from one patient on defibrillation outcome prediction, when used for the development of an Expectation-Maximization Gaussian Mixture Model (EM-GMM)-based bayesian classification model to discriminate "Success" *versus* "No Success" at 5 s post-shock.

2. Material

2.1. Data collection

This study was applied to a collection of ECG recordings from 136 first shocks (Group1) and from 382 second and later shocks (Group2). All victims underwent an Out-of-Hospital Cardiac Arrest (OHCA) intervention with Automated External Defibrillators (AEDs) (Fred and Fred Easy, Schiller Medical SAS, France) used for first-aid by fire fighters in the region of Nancy, France, between July 2006 and September 2009. These observational data were collected retrospectively without any patient identifiable information.

The Nancy Emergency Medical Service (EMC) is a two-tiered system serving urban, suburban and rural portions (714,000 inhabitants). AEDs were used by the first-tier, which consisted of fire brigades all trained in basic life support and defibrillation.

The FRED®Schiller Medical AEDs have a pulsed biphasic defibrillation waveform embedded and followed the ERC 2005 guidelines, with a fixed 150 J energy protocol. For each patient, the defibrillation pads of the AED were applied to the chest (lead II) and were also used for continuous recording in the AED memory.

2.2. Data annotation

For each patient, the first shock delivered on a VF rhythm was included in the Group1 and the second and later shocks were included in the Group2. The 5 s post-shock rhythms were annotated by two biomedical engineers and a cardiologist-electrophysiologist and are summarized in Table 1. The definition of the 5 s post-shock rhythms is:

- Organized Rhythm (OR): Presence of one or more complexes,
- Ventricular Fibrillation (VF): Coarse VF with Peak-to-Peak (PtP) amplitude $\geq 200\ \mu$V,
- Asystole (ASYS): PtP amplitude $< 100\ \mu$V during more than 4 s or VF with PtP amplitude $< 200\ \mu$V

A defibrillation was regarded as successful when VF was converted into an OR 5 s after the defibrillation. A conversion into VF was considered unsuccessful. Two classes were defined: ω_1 the "Success" class and ω_2 the "No success" class. Further will be discussed the reason why we consider to study ω_1=OR *versus* ω_2=VF, without considering the ASYS rhythms.

Table 1. 5 s post-shock rhythms included in Group1 and Group2 and the classification ω_1 *versus* ω_2 with ω_1 the "Success" class and ω_2 the "No success" class.

	Group1	Group2	Classification
OR	32	131	ω_1
VF	22	108	ω_2
ASYS	82	143	

3. Methods

3.1. ECG pre-processing and analysis

The sampling rate of the ECG recorded by the AED was 250 Hz. To obtain measurements that were free of artefacts, each 4.1 s (1,025 samples) ECG epoch immediately before the shock was analyzed. This analysis was conducted off-line using Matlab™(The Mathworks, Inc., Natick, MA, USA). Pre-processing of the ECG recording consisted of a Butterworth first order band-pass 0.5-30 Hz filtering. We evaluated 4 VF morphological features (see Table 2): Mean Slope (MS) from time domain and Detrended Fluctuation Analysis (DFA) parameters from non-linear dynamics. DFA is related to fractal dimension, which is an index for describing the irregularity of signal by measuring patterns of self-similarity. Moreover DFA can be applied on non stationary data sets. DFA plot is not strictly linear but consists of 2 distinct regions of different slopes (DFASlope1 and DFASlope2). The breakpoint with coordinates (DFAFreq, DFAAmp) gives the frontier between the 2 zones.

Table 2. The 4 morphological features: 1 from time domain, 3 from non-linear dynamics.

Domain	Features
Time	Mean Slope (MS) [7–9]
	DFA Slope 2 (DFASlope2) [15, 16]
Non-linear dynamics	DFA Frequency (DFAFreq)
	DFA Amplitude (DFAAmp)

3.2. Classification method

To approach the problem of classification we propose to first learn a set of class-conditional probability density functions, expressed as $P(\overrightarrow{v}/\omega)$, where $\overrightarrow{v}$ is the vector of predictors and ω is a class. An appropriate representation of a class-conditional probability is a Gaussian Mixture Model (GMM) [20]. A GMM is a density function that can be defined as a weighted sum of multivariate gaussian density functions $f(\overrightarrow{v}/\overrightarrow{\mu}_k, \Sigma_k)$ with mean $\overrightarrow{\mu}_k$, covariance matrix Σ_k and α_k the weight of the k^{th} component of the mixture (Equation 1).

$$P(\overrightarrow{v}/\omega) = \sum_{k=1}^{K} \alpha_k f(\overrightarrow{v}/\overrightarrow{\mu}_k, \Sigma_k) \qquad (1)$$

Expectation-Maximization (EM) algorithm combined to GMM is a reliable and scientifically well documented density estimation algorithm [20] (see Figure 1). EM is used for fitting the GMM to a set of training data. In comparison with the standard histogram technique or its alternative the Kernel Density Estimation (KDE) used in other studies [21], EM solved the problem of bins width and smoothing parameter choice. As EM requires prior knowledge of the model order, the optimal K for each class was obtained so as to maximize the likelihood of the data given the model. Once we have learned $P(\overrightarrow{v}/\omega_i)$ with i=1,2 from the training data, we can use the Bayes decision rule (Equation 2) to classify observations from validation database.

$$P(\omega_i/\overrightarrow{v}) = \frac{P(\overrightarrow{v}/\omega_i)P(\omega_i)}{P(\overrightarrow{v})} \tag{2}$$

$P(\overrightarrow{v})$ is the prior probability. So the decision rule minimizes the probability of misclassification by deciding that $\overrightarrow{v}$ predicts a success if $P(\omega_1/\overrightarrow{v}) > P(\omega_2/\overrightarrow{v})$.

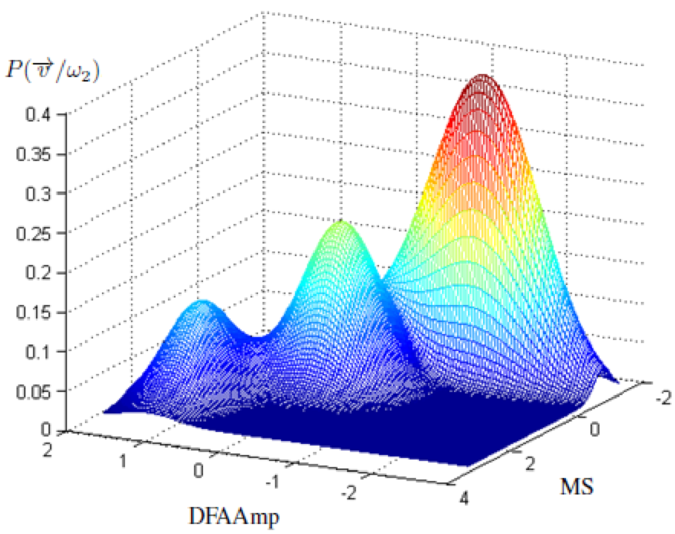

Figure 1. EM-GMM based estimate of the class conditional probability $P(\overrightarrow{v}/\omega_2)$ with $\overrightarrow{v} = (MS, DFAAmp)$.

3.3. Statistical analysis

A cross-validation, more precisely a N-times hold-out method, was run. At each iteration the data were split into two databases: 2/3 for training and 1/3 for testing. Receiver Operator Characteristics (ROC) curves, which represent classifier performance, Sensitivity (Se) and Specificity (Sp) across the range of possible thresholds of likelihood ratio, were constructed. The Area Under the ROC Curve (AUC) represents condensed information regarding discriminating power, usually taking a classifier to be good if AUC > 0.8 and poor if AUC < 0.7. AUC and associated 95% Confidence Intervals (CIs) were calculated.

4. Results

The predictor vector used to analyze both Group1 and Group2 was $\overrightarrow{v}$=(MS, DFASlope2, DFAFreq, DFAAmp). ROC curves enable to compare Group1 and Group2 by observation of the performances of the model to discriminate the 2 classes ω_1 and ω_2 (see Figure 2). For each ROC curve the best balance between Se and Sp are shown in Table 3.

Table 3. Best balance between Se and Sp extracted from ROC curves of the EM-GMM-based bayesian classification and the corresponding AUC with associated 95% CIs.

	Se	Sp	AUC (CI 95%)
Group1	**71.4**	**89.1**	**0.82** **(0.79-0.84)**
Group2	60	63.6	0.65 (0.63-0.66)

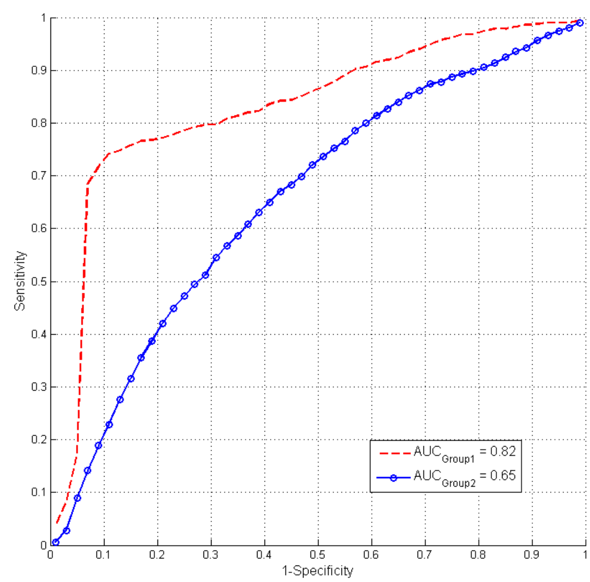

Figure 2. ROC curves for the classification OR *versus* VF considering data from Group1 (in red dotted line) or data from Group2 (in blue solid line with circles).

5. Discussion and conclusions

When considering successive shocks from one patient (Group2), to discriminate classes ω_1 and ω_2, we assist to a decrease in the performances. AUC drops from 0.82 (95% CI 0.79-0.84) to 0.65 (95% CI 0.63-0.66), that leads to suppose the presence of a random component, that is certainly characteristic of an intra-patient correlation. Indeed, Group2 is including longitudinal data, because several shocks are coming from a same patient over time.

It has been proposed to analyze OR *versus* VF, because it is suspected that ASYS subset is a grey area that is more difficult to discriminate. But ASYS shock outcome makes up 60% of the episodes for Group1 and 37% of the episodes for Group2, that's why the observations made on our results should be considered as a first step to be reconfirmed with a new and more consistent database.

The proposed Gaussian Mixture Model (GMM)-based bayesian classifier hold promise for predicting the first defibrillation outcome at 5 s post-shock. When applying the classifier to longitudinal data, within-patient correlation affects the prediction accuracy. For clinical application, ASYS rhythm remains a grey area, which still requires further investigations.

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