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Prediction of Defibrillation Outcome by Ventricular Fibrillation Waveform Analysis: A Clinical Review

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Abstract

The most frequent initial rhythm in out-of-hospital witnessed cardiac arrest is ventricular fibrillation (VF) and electrical defibrillation is still the only effective therapy for the termination of this life-threatening cardiac arrhythmia. Even though earlier defibrillation is greatly emphasized during cardiopulmonary resuscitation (CPR), unnecessary or repetitive high energy defibrillations are associated with decreased post-resuscitation myocardial function. Optimizing the timing of defibrillation is of great importance in order to discriminate patients should receive immediate defibrillation versus alternate therapies such as CPR. Since characteristics of VF waveform changes over time and with CPR, which exhibit predictable ability of defibrillation success, quantitative analysis of VF waveform has the potential to guide defibrillation. This article reviewed methods developed for VF waveform analysis (including time domain, frequency domain, time-frequency domain, nonlinear analysis, and combination analysis techniques) and their performances for the prediction of defibrillation outcomes in clinical settings. The retrospective meta-analysis confirmed that VF waveform could predict the return of organized electrical activity, restoration of spontaneous circulation, and survival reliably. Additionally, predictors based on time-frequency and nonlinear methods were superior to other methods on the whole. However, no prospective studies have been performed to identify the optimal time of defibrillation utilizing VF waveform analysis until now. Therefore, the value of VF waveform analysis to guide clinical countershock management still needs further investigation.

Keywords: Cardiac arrest; Ventricular fibrillation; Waveform analysis; Defibrillation prediction

Introduction

Ventricular fibrillation (VF), which is characterized as rapid and disorganized contractions of the heart with complex electrocardiogram (ECG) patterns, is the most frequent initial rhythm in out-of-hospital witnessed cardiac arrest (CA) [1]. Electrical defibrillation, which consists of delivering of a therapeutic dose of electrical current to the fibrillating heart with the aid of a defibrillator, is still the only effective way to treat this life-threatening arrhythmia [2]. The probability of defibrillation success is inversely proportional to the duration of VF. Clinical data reported that for every minute passes between collapse and defibrillation, survival rates from witnessed VF decrease 7% to 10% if no cardiopulmonary resuscitation (CPR) is provided. With effective CPR, the success rate of rescue decreases 3-4% per minute [3]. Thus, early CPR together with early defibrillation is a key point in the chain of survival.

The fundamental importance of early defibrillation as a major predictor of outcome in patients with VF has been known since the introduction of external defibrillators [4]. However, emerging evidence showed that not all patients in VF might benefit from being treated in the same manner. Both animal and human studies demonstrated that defibrillation immediately after the onset of VF usually resulted in restoration of spontaneous circulation (ROSC). However, when the duration of untreated VF exceeded 4-5 minutes, initial CPR with chest compression before delivery of a defibrillation attempt improved the likelihood of restoring an organized cardiac electrical activity with pulses [5,6]. Unnecessary shocks can reduce chest compression time and can cause VF to deteriorate into asystole or pulseless electrical activity, which is more difficult to resuscitate [7,8]. On the other hand, repeated futile defibrillation attempts with high energy also associated with myocardial damage and resulting in reduced chance of survival [9]. For these reasons, the ability to gain information concerning the metabolic state of the myocardium and to optimize the timing of defibrillation would be of enormous benefit in allowing therapy to be tailored to an individual heart.

The optimal timing of defibrillation can be determined by evaluating the probability of shock outcome. If the shock attempt has a high likelihood of defibrillation success, an electrical shock should be prompted and delivered. Otherwise, unnecessary shocks should be avoided and alternate therapy such as CPR or medications, especially high-quality chest compression, should be utilized. Earlier investigations established that both the coronary perfusion pressure (CPP) and the end-tidal carbon dioxide ($PetCO_2$) could serve as measurements of the effectiveness of chest compression and therefore as predictors of the likelihood of ROSC [10,11]. But real-time measurements of CPP and $PetCO_2$ are not widely available during out-of-hospital settings.

ECG waveform, which is routinely available in the current automated external defibrillators (AEDs), has been extensively investigated for the purpose of predicting the probability of defibrillation outcome [12]. The ECG signals recorded from the body surface represent the superposition of all of the electrical fields generated by each volume element of the heart [13]. Presumably, the organization of the surface ECG has some relationship to the underlying organization of the myocardial electrical activity. Since characteristics of VF waveform change over time and with CPR, which exhibits ability for prognostication of defibrillation

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success, the quantitative analysis of VF waveform has the potential to be used to predict the VF duration and the probability of shock outcome, to optimize the timing of defibrillation, and to ultimately guide CPR interventions [14].

The observation that defibrillation success rate is higher during the initial period of CA where "coarse VF" with an amplitude greater than 0.2 mV is present, while success of defibrillation is greatly reduced at this stage of "fine VF", is finally evolved to extensive quantitative analysis of ECG waveform [15]. Earlier animal studies demonstrated that duration of CA and defibrillation outcome can be predicted from amplitude and frequency variables obtained from VF waveform [16-19], where the experimental conditions about animals were convenient to be controlled [20]. With widely application of AEDs, various VF analysis techniques, including time domain, frequency domain, time-frequency domain, nonlinear analysis, and combination analysis techniques, have been adapted and developed to predict the probability of defibrillation outcome for patients who experienced out-of-hospital cardiac arrest (OHCA) [21]. In the past 20 years, considerable efforts have been made to further improve the predictive power of rescue shock measures. However, no prospective clinical study has been performed to validate the predictability of VF waveform with real-time analysis. This article reviews the methods used for VF waveform analysis and their performances for the prediction of defibrillation outcomes in clinical settings. The purpose of this study is to compare the advantages of different methods and their reliabilities for optimizing the timing of defibrillation in OHCA patients with retrospective meta-analysis.

Literature Searches

An automatic search was conducted of the following electric databases: *PubMed*, *EMBASE*, *Web of Science*, *ScienceDirect*, and *IEEEXplore*, with the keywords such as "defibrillation prediction", "ventricular fibrillation", "waveform analysis", "clinical", and "success countershock". In addition to these automated searchers, a manual search of key articles was conducted as well. All researches published between January, 1985 through March, 2013 were considered. Only papers published in English were included. As a result, a total of 186 literatures were obtained.

For study selection, the publications about myocardial infarction, atrial fibrillation, coronary artery, acute myocardial, waveforms of AEDs, and patients with implantable cardioverter defibrillators (ICDs) were excluded. Moreover, publications focused on the detection of shockable waveform rather than prediction of defibrillation success were also excluded [22,23]. Of the rest literatures, 1 repeated study was removed. As a result, a total of 33 studies that met our selection criteria were finally evaluated. Among the 33 studies, 14, 2, 2, and 2 were published in *Resuscitation*, *Circulation*, *Annals of Emergency Medicine*, and *Anesthesia and Analgesia*, respectively; the rest 13 studies were published in other medicine journals.

Methods for VF Waveform Analysis

The procedure for the prediction of defibrillation outcome using VF waveform analysis is shown in Figure 1. An episode VF signal with the duration of 1 to 10 seconds, which is immediately before the shock delivery, is usually selected from the surface recording. Due to the fact that preshock pause was independently associated with a decrease in defibrillation efficacy [24], and the recommendation that the delivery of a shock should be achieved with an interruption in chest compressions of no more than 5 seconds by European Resuscitation Council [25] , CPR artifacts may present in the recorded ECG signals.

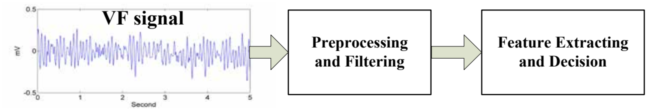

Figure 1: The flowchart of the prediction of defibrillation using waveform analysis

Additionally, the ECG signals recorded from AEDs may also include baseline drifts, powerline interferences, muscle movements, and so on [26-28]. A preprocessing step is usually employed to obtain the 'pure' ECG signals before the waveform analysis, including a notch filter to remove alternating current interference at 50-60 Hz, a high-pass filter to remove baseline drifting and CPR artifact, and a low-pass filter to remove the myographic noise [29-34]. After filtering, the features or characteristics of the VF signal extracted with different digital signal processing methods are then used to predict the probability of defibrillation success based on the established threshold or decision algorithm.

Based on the digital processing technologies are used, the methods or algorithms used to predict the shock outcome can be categorized into the following five groups: time domain methods, frequency domain methods, time-frequency domain methods, non-linear dynamic methods of randomness and complexity, and the combination of different methods.

Time domain methods

Predictors obtained from time domain describe the characteristics of waveform amplitudes, phases or voltages. Peak-to-peak amplitude (PPA), which is defined as the difference between the maximum and minimum recorded ECG voltage within a given window, was shown to be a powerful indicator of defibrillation outcome by Weaver et al. [15]. Monsieurs and colleagues proposed a survival index, which is calculated as the weighted sum of the VF amplitude and the number of base-line crossings per second, to discriminate potential survivors from non-survivors [35]. The mean amplitude, representing the mean absolute deviation from the mean of the waveform, was used to predict ROSC by Hamprecht and colleagues [36]. Median slope (MdS) and mean slope (MS), which represent the average steepness of the waveform, reflect both the amplitude and frequency information of VF. Joar et al. [37] analyzed the median slope (MdS) in relation to VF duration and the rhythm before onset of VF, which indicated MdS could be used for shock outcome prediction. Neurauter and colleagues studied MdS and MS originated from a range clearly above a lower edge frequency to predict the shock outcome [38]. The extrema of phases, which are defined as the phases of a VF interval immediately before countershock, were found to be sinusoidal with the probability of success defibrillation attempts by Suzuki and colleagues [39].

Amplitude, slope, and phase of VF are not only dependent on the duration of VF but are also affected by other factors: interference, physique, skin resistance, size and position of electrodes, lead ways, and recording conditions [13]. Additionally, the time domain methods do not utilize the temporal information to predict the defibrillation [40]. For these reasons, time-domain features or characteristics are probably crude predictors of defibrillation.

Frequency domain methods

Frequency domain features describe the frequency component characteristics of VF waveform. Each frequency component, representing globally averaged information, is computed over the clipped ECG segment. The calculated features from the fast Fourier transform (FFT) of VF signals, such as peak power frequency (PF) or dominant frequency (DF) [36,41-45], energy [38,46], maximum power (maximum value of the power spectral density (PSD)), power spectrum area (PSA), centroid power [38] , centroid frequency(FC) [38,44,46,47], median frequency(MF) [45,48,49], spectral flatness measure, fibrillation power, instantaneous mean frequency, frequency ratio and amplitude spectrum area (AMSA) [38], were shown to be capable of predicting defibrillation success.

PF (DF), which is defined as the highest peak in the resulting spectral density, was shown to be predictable of the countershock success by Stewart et al. [41]. FM is calculated as the mean of all of the contributing frequencies weighted by the power at each frequency and was found to be predictive shock outcome by Martin et al. [50]. The energy calculated by adding up the single power values of the PSD, was adopted to predict defibrillation outcome of VF [46]. FC, which is defined as frequency coordinate of the center of the spectral mass, served as a predictor of the success of electrical defibrillation as well [38,44,46,47]. Similarly, centroid power, which is defined as power coordinate of the center of the spectral mass, was used to predict the countershock success by Neurauter et al. [38], Hamprecht et al. [36] defined the fibrillation power as integral over the fibrillation contribution to the PSD and compared its performance with dominant frequency and mean amplitude. AMSA, calculated as the sum of contributing frequencies weighted by the absolute values of the Fourier transform of the VF signal, describes the amplitude-weighted mean frequency. AMSA was found to be positively related to the probability of successful restoration of cardiac rhythm by Young et al. [51]. Neurauter and coauthors [52] evaluated the predictabilities of PSA, which is computed in a similar way to AMSA using PSD instead of amplitude spectral density, and other features from different sub-bands of VF in a retrospective clinical study.

Frequency domain features are robust and less affected by external factors than the time-domain features [53]. The fundamental problem of frequency domain methods is that FFT analysis is only suitable for stationary signals whereas the ECG signals are non-stationary and non-linear.

Time-frequency domain methods

The continuous or discrete wavelet transform resolves the weakness of frequency domain analysis by providing concomitant spectral and temporal information, allowing a local scale-dependent spectral analysis of signal features. Wavelet-based PF, energy, mean frequency, spectral flatness, and entropy were investigated by Watson and colleagues to predict shock outcome using Bayesian statistics [54].

Cardioversion outcome prediction (COP) (i.e. the wavelet-entropy marker), which is used as a metric of the temporal behavior of the signal, can provide an index for the defibrillation identification by Watson and colleagues [49]. Box et al. [55] adopted COP to analyze the ECG data record and provided confidence in the robustness of the technique across hardware platform. Gundersen et al. [47] also adopted COP, which yielded the best mixed effects models, for shock outcome prediction.

The total mid-band (3–10 Hz) energy spectrum analysis based on continuous wavelet transform was studied by Endoh and colleagues using logistic regression analysis to predict defibrillation [40]. Features from dual-tree complex wavelet domain were developed for defibrillation outcome prediction by Shandilya and colleagues [28].

Non-linear dynamic methods

Earlier researches confirmed that VF is a complex non-linear pattern formed by drifting spiral waves of electrical activity (vortices and rotors) that travel across the myocardium and subsequently break down [56,57]. VF waveform may actually be produced by deterministic mechanisms characteristics of dynamic non-linear system. Early VF was shown to contain an 80-90% deterministic component by a complex mathematical algorithm [58]. There are several reported non-linear features to predict VF defibrillation success, such as the scaling exponent (ScE), Hurst exponent, the logarithm of the absolute correlations (LAC), self-similarity dimension, and detrended fluctuation analysis (DFA).

The ScE is an estimate of the fractal self-similarity dimension. Callaway and colleagues [59] assessed the ability of ScE to predict the success of defibrillation. The Hurst exponent, which is used as a measure of long term memory of time series, was included in a model to predict successful defibrillation attempts by Podbregar et al. [60]. Irregularity, which is a direct indicator of chaotic behavior, was found to be associated with successful defibrillation by Jagric and colleagues [61]. LAC, which quantifies how individual parts of a signal are self-similar at different points along its length, was proposed by Sherman and coauthors to provide prognostic information regarding the duration of VF by measuring the roughness of the VF waveform [62]. DFA, which determines the statistical self-affinity of VF waveform, was used to assess the duration of a VF crisis by Rodriguez et al. [63]. Lin and coauthors [64] applied the DFA on the VF signal analysis to predict the defibrillation success.

Though the VF waveform analysis based on the dynamic non-linear achieved some improvement in predicting successful defibrillation, the non-linear dynamic method is sensitive to the noise and interference.

Combination of several methods

The combinations of individual measurements based on different methods above have also been employed to predict shock outcome. Brown et al. [44] carried out a retrospective analysis of VF signals using 4 features and reported that the combination of FC and PF performed better than other combination and may be used to predict countershock success or to guide therapy during CA. Jekova [65] analyzed a set of 10 parameters reflecting the frequency characteristics, the variations, the complexity, the periodicity and the symmetry of the ECG signals using linear discriminant functions of the 10-dimensional vector. Gundersen and colleagues [47] analyzed 6 predictive features: AMSA, MS, MdS, COP, mean amplitude, and FC using the complete recordings of ECG waveforms. Random effects for each single ECG-feature and the best combination of features performing a forward and a backward search were tested, respectively.

Eftestøl and colleagues [43,46] combined two decorrelated spectral features based on the principal component analysis (PCA) of an original feature set with information on FC, peak power frequency, spectral flatness and energy, using multidimensional information in a single reproducible variable reflecting the probability of defibrillation success. Watson and colleagues [54] analyzed the performance gained through the combination of PF, energy, mean frequency, spectral flatness, and entropy measure, when PCA was applied to the combination of features.

Podbregar and colleagues [60] studied the predictive power of a model developed by genetic programming (GP) on the complete VF database including maximal amplitude, total energy of power spectral density, and the Hurst exponent to predict defibrillation success.

Neurauter and colleagues [38] applied neural networks on single-feature combinations to optimize the prediction of countershock success. Time domain features (e.g. mean amplitude, PPA, and MS) and frequency domain features (e.g. PF, centroid power, and the PSA) were calculated from the re-countershock VF ECG signal. Shandilya and colleagues [28] focused on time-series and complex wavelet integration of multiple features through machine learning techniques, training and testing 6-10 features for each test fold with nested 10-fold cross validation. Identification of the most discriminative features and correlated variables were conducted by the supervised feature selection. A parametrically optimized support vector machine model was trained for predicting outcomes.

The combination method synthesizes several single features by linear discriminant functions, neural networks, GP, and so on. Thus, the computing power is prodigious and time consuming, which may not satisfy the computational requirement of AEDs.

Results

Definition of defibrillation success

There is no consistent definition of defibrillation success of the related publications [28]. According to the literatures, two definitions were commonly adopted in the studies of countershock prediction as standard of successful defibrillation: (1) defibrillation was considered to be successful with resulting in an organized rhythm seen at 5 second after delivery of the shock regardless of palpated pulsation of the common carotid artery by Koster et al. [66]; (2) successful defibrillation was defined as those attempts which result in ROSC sustained for a period greater than 30 seconds and originating within a minute of the applied shock by Watson et al. [49].

In this clinical review, we broadly classify outcomes into three categories based on the definitions of defibrillation success in each article. The first one is return of organized electrical activity (ROEA) at least 5 seconds following countershock including termination of the VF and return of a stable supraventricular rhythm, termed as Definition 1. The second one is ROSC, which generates a pulse regardless of the duration at least 30 s without continuing CPR, termed as Definition 2. The palpated pulsation of the common carotid artery is an important sign of ROSC differing from the ROEA. The third one is the most rigorous definition, as the survival at least 6 hours after resuscitation or with discharge from the hospital, termed as Definition 3.

According to the three categories of definition of successful defibrillation, the clinical performances of defibrillation predictors are listed in the following three tables. Table 1 corresponds to Definition 1, Table 2 presents the results according to Definition 2, and Table 3 shows the performances using Definition 3. Only the predictor with the best performance is listed in the three tables, if several predictors were analyzed in one study.

Retrospective analysis results

Results of different defibrillation prediction methods in the literatures are commonly presented in terms of sensitivity, specificity, and area under receiver operating curve (ROC) curve (AUC). Sensitivity is defined as the proportion of shocks that are successfully defibrillated which are correctly identified, specificity is the proportion of failed shocks that are correctly identified [49], and AUC is defined as the area under the ROC curve. A trade-off in sensitivity and specificity achievable by a system is described by plotting sensitivity/specificity pairs in a ROC curve. AUC provides an indication of the system effectiveness. The larger the AUC value is, the better the system performance presents. An ideal case is that an area equals to unity where sensitivity is one for all specificities. Other unusually criteria such as the accuracy [28], the odds ratio (OR) [67], and the Wald value [40] that adopted to evaluate the performances of different defibrillation predictors were not analyzed in our results.

A total of 7 studies reported their data according to Definition 1 (Table 1). Sensitivity ranges from 61% to 100% with an average value of 87.4%, specificity ranges from 14% to 97% with the averaged value 55.3%. Among the 7 features, MF, PPA, PF and a combination by GP achieve the highest sensitivity 100%. A combination by GP achieves the highest specificity 97%. Two studies reported their results of AUC, with 0.65 for DFA and 0.77 for FC based on CWT.

A total of 20 studies reported their data according to Definition 2 (Table 2). Sensitivities range from 59% to 100% with the averaged value 89.7%. COP and a combination of PF and FC achieve the highest sensitivity of 100%. Specificities range from 32% to 97% with the averaged value 61.2%. Among the 14 investigated features, AMSA achieves the highest specificity of 97%. AUC values range from 0.77 to 0.94 with the averaged value 0.86. The feature based on complex wavelet transform with addition of the $PetCO_2$ signal achieves the highest AUC of 0.94.

A total of 6 studies reported their data according to Definition 3 (Table 3). Sensitivities range from 54% to 96.7% with the averaged value 78.4%. PPA achieves the highest sensitivity 96.7%. Specificities range from 22.7% to 98% with the averaged value 70.7%. Among the 5 investigated features, PPA achieves the highest specificity 98%. The only reported AUC value is 0.84 achieved by SE.

Meta-analysis (Review Manager 5.2.4) was utilized to evaluate the effects of successful defibrillation definition and methods used for VF waveform analysis on the performance of the predictability. All of the predictors were included for meta-analysis to enhance the reliability if more than 1 indicator was investigated for each study.

The results of meta-analysis based on the definition of defibrillation success are listed in Table 4. Characteristics of VF waveform can reliably predict defibrillation outcome with the use of definition of ROEA, ROSC and survival. The odds ratio (OR) for prediction of ROEA is significantly higher than those of ROSC and survival. The results listed in Table 5 revealed that time-frequency and nonlinear methods outperformed other techniques with relative higher OR when ROSC is served as shock outcome.

Discussion

The duration of VF is a major determinant of counter shock outcome. However, it is difficult to establish the prior duration of VF in clinical settings. An ideal predictor of defibrillation shock outcome would enable the rescuers to provide the most appropriate therapy for the patient, and could be implemented into existing AEDs with less computing power. Many clinical studies have been performed to measure the characteristics of VF waveform and predict the likelihood of successful defibrillation. However, there is still no clinical standard has been postulated as the threshold of the reliability of shock prediction.

A sensitivity of 95% and specificity of 50% was suggested as safe and useful predictor for the treatment of VF by Neurauter et al. [38,73]. Based on the reported results, a combination of PPA, total energy of PSD and Hurst exponent with GP algorithm outperformed other indicators for the prediction of ROEA, with a sensitivity of 100% and specificity

Year	Author	Predictor	Data	AUC	SES(%)	SPE(%)
1991	Dalzell et al. [68]	PPA	70 patients within or outside hospital	/	/	/
1994	Strohmenger et al. [48]	MF	20 patients during aortocoronary bypass grafting	/	100	/
1997	Strohmenger et al. [45]	PPA and PF	26 patients with OHCA	/	100	25
2003	Podbregar et al. [60]	Combination of PPA, total energy of PSD and Hurst exponent by GP	47 patients with OHCA (79 success shock, and 124 unsuccess shock)	**/**	**100**	**97**
2010	Lin et al. [64]	DFA(DFAα2)	155 OHCA subjects (37 successful and 118 unsuccessful defibrillations)	0.65	61	63.2
2011	Endoh et al. [40]	FC based on CWT	152 patients with OHCA(164 unsuccessful and 69 successful episodes)	0.77	76.8	62.8
2012	Shanmugasundarama et al. [67]	Slope	44 patients with OHCA: In recurrent VF	/	91	14
			In shock-resistant	/	83	70

SES, sensitivity; SPE, specificity; "/ " denotes the corresponding values were not reported.

Table 1: Performance of defibrillation predictors using Definition 1.

Year	Author	Predictor	Data	AUC	SES(%)	SPE(%)
1991	Martin et al. [50]	MF	7 patients	/	/	/
1996	Brown et al. [44]	Combination of PF and FC in certain ranges	55 patients with OHCA	/	100	47.1
2000	Eftestol et al. [46]	Combination of FC and PF	156 patients with OHCA (total 868 shocks:87 had caused ROSC and 781 had failed to cause ROSC)	/	92 ± 2	42 ± 1
2001	Strohmenger et al. [69]	DF	89 patients with OHCA	/	92	42
2001	Eftestøl et al. [43]	Combination of CF and the energy	156 patients with OHCA (total 883 shocks:87 had caused ROSC and 781 had failed to cause ROSC)	/	91 ± 3	36 ± 4
2001	Hamprecht et al. [36]	DF	54 patients with OHCA (artefact-free ventricular fibrillation episodes, 28 return to ROSC)	/	59	52
2004	Jekova et al. [70]	Energy between 2 and 7 Hz	more than 700 out-of-hospital fibrillation cases	/	61.8	79.6
2004	Young et al. [51]	AMSA	46 patients with OHCA	/	91	94
2004	Watson et al. [54]	Entropy measure based on Morlet wavelet	87 success shock and 781 unsuccess shock	/	91 ± 2	60 ± 6
2005	Watson et al. [49]	COP based on a tunable Morlet wavelet	110 patients with OHCA	/	97 ± 2	63 ± 4
2006	Watson et al. [71]	COP based on CWT	110 patients with OHCA	/	95 ± 4	66 ± 4
2007	Neurauter et al. [38]	MdS	197 patients with in-hospital and out-of-hospital CA	0.848	95.2	52.6
2007	Jagric et al. [61]	Irregularity	120 recordings of VF	/	/	/
2008	Gundersen et al. [47]	COP	86 patients with OHCA	0.877	/	/
2008	Box et al. [55]	COP based on wavelet transform	54 patients with OHCA	/	100	60
2008	Sherman et al. [62]	LAC	158 patients with OHCA	0.77		
2008	Ristagno et al. [72]	AMSA	90 patients with OHCA	/	91	97
2008	Neurauter et al. [73]	MdS(10-22Hz)	192 patients with in-hospital and out-of-hospital CA	0.863	95.2	49.7
2012	Nakagawa et al. [74]	AMSA	83 patients with OHCA	/	94	59
2012	Shandilya et al. [28]	Feature based on complex wavelet transform	57 patients (34 successful and 56 unsuccessful defibrillations) ECG signals without addition of the PetCO2 signal	0.850	90	78.6
			With addition of the $PetCO_2$ signal	0.938	/	/

SES, sensitivity; SPE, specificity; "/ " denotes the corresponding values were not reported.

Table 2: Performance of defibrillation predictors using Definition 2

Year	Author	Predictor	data	AUC	SES(%)	SPE(%)
1985	Weaver et al. [15]	PPA	394 patients	/	96.7	22.7
1992	Stewart et al. [41]	PF	56 patients in hospital and in the community	/	/	/
1998	Monsieurs et al. [35]	Survival index	100 patients with OHCA	/	79	70
			If adding age	/	86	73
2003	Goto et al. [42]	DF	47 patients with OHCA	/	76.5	90
1993	Callaham et al. [75]	PPA	265 patients in prehospital VF	/	54	98
2001	Callaway et al. [59]	SE	75 subjects with OHCA	0.84	/	/

SES, sensitivity; SPE, specificity; "/ " denotes the corresponding values were not reported.

Table 3: Performance of defibrillation predictors using Definition 3.

Definition	Number of study	OR (95% CI)	P value
Definition 1 (ROEA)	7	0.72[0.58 0.89]	0.003
Definition 2 (ROSC)	20	0.52 [0.41 0.67]	<0.001
Definition 3 (Survival)	4	0.50 [0.38 0.65]	<0.001

Table 4: Results of meta-analysis based on the definition of defibrillation success

Methods	Number of study	OR (95% CI)	P value
Time domain	3	0.52 [0.37 0.74]	<0.001
Frequency domain	7	0.56 [0.35 0.90]	0.02
Time-frequency	4	0.69 [0.56 0.84]	0.003
Nonlinear	1	0.66 [0.48 0.92]	0.01
Combination	3	0.20 [0.07 0.58]	0.003

Table 5: Results of meta-analysis of different methods based on Definition 2 (ROSC)

of 97% [60]. MdS [38,73], AMSA [74], and COP based on wavelet transform [49,55,71] could reliably predict ROSC with a sensitivity of 95% and specificity above 50%. Whereas no indicator could predict survival with a sensitivity of 95%, even all of the reported specificities were above 50%. A shortcoming of direct comparison of sensitivity and specificity is the trade-off in threshold selection for the classification. As the ability to correctly identify successful shocks increases, the proportion of correctly identified failed shocks will decrease. For this reason, a balance between sensitivity and specificity and both above 70% may be considered as a reliable predictor, such as AMSA [72] and slope [67] for the prediction of ROEA, AMSA [51] and features based on complex wavelet transform [28] for the prediction of ROSC, and survival index and DF for the prediction of survival.

The AUC, which represents the expected performance of a binary classifier system with a single value, does not affected by the selected threshold. Among the studies that reported AUC, MdS [38,73], COP [47] and feature based on complex wavelet transform [28] for the prediction of ROSC, and SE [59] for the prediction of survival outperformed other methods with an AUC value great than 0.80.

The meta-analysis confirmed these results. The time-frequency and nonlinear methods perform better than methods based on time domain, frequency domain and the combinations [59,60,64]. Predictors based on wavelet transform are superior to the frequency predictors and the nonlinear predictors [28, 40,47,49]. Even though a previous study reported that the combination of decorrelated features presented better performances than a single feature [44,46], meta-analysis based 3 combination methods in Table 5 shows that combination of single predictive features does not improve outcome prediction, which is consistent with Neurauter's result [38].

The preprocessing algorithms may also affect the accuracy of shock outcome prediction. The filtered ECG signals or CPR-artifact-free ECG signals presented better results than the ECG signals with CPR artifacts and without preprocessing [73]. Moreover, some studies employed peripheric information, e.g. age, sex, and $PetCO_2$ signal, to enhance the performances of defibrillation predictors [28,35].

From the results in Tables 1-3, we can see that the highest sensitivity/specificity pair is achieved with the definition of ROEA (in bold). The meta-analysis results shows that a better performance is obtained with the definition of ROEA for the prediction of defibrillation outcome compared with those of and ROSC and survival. The reason is that Definition 1 includes the case of ROSC, which means patients who achieved an organized cardiac rhythm may fail to ROSC. Similarly, Definition 2 includes the case of survival and discharge from hospital since patients who achieve ROSC may die within a few hours due to post-resuscitation cerebral injury and myocardial dysfunction. Post-resuscitation care interventions such as therapeutic hypothermia can significantly improve both the neurological recovery and survival after resuscitation from CA.

Limitation

There are several limitations need to be addressed for this review analysis. Firstly, the durations of VF waveform that used to be analyzed are different from individual studies. According to the reported results, an episode of 1 to 10 seconds is usually selected from the surface ECG. However, effect of window length on the performance has not been systematically investigated. Secondly, although the filtered ECG signals or CPR-artifact-free ECG signals are reported to have better results than the ECG signals with CPR artifacts and without preprocessing, whether the application of different filtering methods, such as adaptive filtering improve the predictability is still unknown. Thirdly, the waveform design is significantly differ among manufactures, therefore the reliability of VF waveform analysis with the use of different defibrillation waveforms needs to be researched. Fourthly, meta-analysis revealed that time-frequency and nonlinear methods are superior to other techniques, but only a few papers present results of direct comparisons between various methods. The interpretation may be biased due to different patient number, analytical measurement and post-shock annotations.

Conclusion

Recent clinical studies verified that it is possible to predict defibrillation success from the VF waveform with varying reliability. Digital signal processing techniques based on amplitude, slope, spectrum, energy, wavelet transform, fractal, entropy, advanced machine learning, and so on, have been applied/proposed to extract features and make decisions for the optimal timing of defibrillation based on surface ECG waveform. Among these techniques, time-frequency and nonlinear methods outperform time domain and frequency domain methods. A better performance is obtained for the prediction of defibrillation success with a short term outcome definition, i.e. ROEA. The combination of single features derived from VF waveform does not further increase the predictability. But the performance of defibrillation predictors may be improved by incorporating patient information and other physiological measurements.

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Conflict of interest statement

The authors have no conflicts of interest to disclose.

References

1. Caffrey SL, Willoughby PJ, Pepe PE, Becker LB (2002) Public use of automated external defibrillators. N Engl J Med 347: 1242-1247.
2. Sternbach GL, Varon J, Fromm RE (2000) The resuscitation greats. Claude Beck and ventricular defibrillation. Resuscitation 44: 3-5.
3. Link MS, Atkins DL, Passman RS, Halperin HR, Samson RA, et al. (2010) Part 6: Electrical Therapies Automated External Defibrillators, Defibrillation, Cardioversion, and Pacing 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 122: S706-S719.
4. Holmberg M, Holmberg S, Herlitz J (2000) Incidence, duration and survival of ventricular fibrillation in out-of-hospital cardiac arrest patients in sweden. Resuscitation 44: 7-17.

5. Wik L, Hansen TB, Fylling F, Steen T, Vaagenes P, et al. (2003) Delaying defibrillation to give basic cardiopulmonary resuscitation to patients with out-of-hospital ventricular fibrillation: a randomized trial. JAMA 289: 1389-1395.

6. Cobb LA, Fahrenbruch CE, Walsh TR, Copass MK, Olsufka M, et al. (1999) Influence of cardiopulmonary resuscitation prior to defibrillation in patients with out-of-hospital ventricular fibrillation. JAMA 281: 1182-1188.

7. Berg RA, Hilwig RW, Ewy GA, Kern KB (2004) Precountershock cardiopulmonary resuscitation improves initial response to defibrillation from prolonged ventricular fibrillation: a randomized, controlled swine study. Crit Care Med 32: 1352-1357.

8. Weisfeldt ML (2004) A three phase temporal model for cardiopulmonary resuscitation following cardiac arrest. Trans Am Clin Climatol Assoc 115: 115-122.

9. American Heart Association (2005) Part 3: Defibrillation. Circulation 112: III-17-III-24.

10. Paradis NA, Martin GB, Rivers EP, Goetting MG, Appleton TJ, et al. (1990) Coronary perfusion pressure and the return of spontaneous circulation in human cardiopulmonary resuscitation. JAMA 263: 1106-1113.

11. Gudipati CV, Weil MH, Bisera J, Deshmukh HG, Rackow EC (1988) Expired carbon dioxide: a noninvasive monitor of cardiopulmonary resuscitation. Circulation 77: 234-239.

12. Strohmenger HU (2008) Predicting defibrillation success. Curr Opin Crit Care 14: 311-316.

13. Callaway CW, Menegazzi JJ (2005) Waveform analysis of ventricular fibrillation to predict defibrillation. Curr Opin Crit Care 11: 192-199.

14. Li Y, Ristagno G, Bisera J, Tang W, Deng Q, et al. (2008) Electrocardiogram waveforms for monitoring effectiveness of chest compression during cardiopulmonary resuscitation. Crit Care Med 36: 211-215.

15. Weaver WD, Cobb LA, Dennis D, Ray R, Hallstrom AP, et al. (1985) Amplitude of ventricular fibrillation waveform and outcome after cardiac arrest. Ann Intern Med 102: 53-55.

16. Noc M, Weil MH, Tang W, Sun S, Pernat A, et al. (1999) Electrocardiographic prediction of the success of cardiac resuscitation. Crit Care Med 27: 708-714.

17. Achleitner U, Wenzel V, Strohmenger HU, Krismer AC, Lurie KG, et al. (2000) The effects of repeated doses of vasopressin or epinephrine on ventricular fibrillation in a porcine model of prolonged cardiopulmonary resuscitation. Anesth Analg 90: 1067-1075.

18. Marn-Pernat A, Weil MH, Tang W, Pernat A, Bisera J (2001) Optimizing timing of ventricular defibrillation. Crit Care Med 29: 2360-2365.

19. Povoas HP, Weil MH, Tang W, Bisera J, Klouche K, et al. (2002) Predicting the success of defibrillation by electrocardiographic analysis. Resuscitation 53: 77-82.

20. Di Maio R, Allen JD, Navarro C, Darragh K, Anderson JM, et al. (2009) Changes in the frequency spectrum, the P-P interval, and the bispectral index during ventricular fibrillation are physiologic indicators of ventricular fibrillation duration. J Electrocardiol 42: 527-533.

21. Hollenberg J, Svensson L, Rosenqvist M (2013) Out-of-hospital cardiac arrest: 10 years of progress in research and treatment. J Intern Med 273: 572-583.

22. Irusta U, Ruiz J, Aramendi E, Ruiz de Gauna S, Ayala U, et al. (2012) A high-temporal resolution algorithm to discriminate shockable from nonshockable rhythms in adults and children. Resuscitation 83: 1090-1097.

23. Ayala U, Irusta U, Ruiz J, Gonzalez-Otero D, Alonso E, et al. (2012) A New Shock Advice Algorithm Designed to Classify ECG Signals During Cardiopulmonary Resuscitation. Computing in Cardiology 39: 25-28.

24. Cheskes S, Schmicker RH, Christenson J, Salcido DD, Rea T, et al. (2011) Perishock pause: an independent predictor of survival from out-of-hospital shockable cardiac arrest. Circulation 124: 58-66.

25. Nolan JP, Soar J, Zideman DA, Biarent D, Bossaert LL, et al. (2010) European Resuscitation Council Guidelines for Resuscitation 2010 Section 1. Executive summary. Resuscitation 81: 1219-1276.

26. Werther T, Klotz A, Granegger M, Baubin M, Feichtinger HG, et al. (2009) Strong corruption of electrocardiograms caused by cardiopulmonary resuscitation reduces efficiency of two-channel methods for removing motion artefacts in non-shockable rhythms. Resuscitation 80: 1301-1307.

27. Werther T, Klotz A, Kracher G, Baubin M, Feichtinger HG, et al. (2009) CPR artifact removal in ventricular fibrillation ECG signals using Gabor multipliers. IEEE Trans Biomed Eng 56: 320-327.

28. Shandilya S, Ward K, Kurz M, Najarian K (2012) Non-linear dynamical signal characterization for prediction of defibrillation success through machine learning. BMC Med Inform Decis Mak 12: 116.

29. Aramendi E, Ayala U, Irusta U, Alonso E, Eftestøl T, et al. (2012) Suppression of the cardiopulmonary resuscitation artefacts using the instantaneous chest compression rate extracted from the thoracic impedance. Resuscitation 83: 692-698.

30. Granegger M, Werther T, Gilly H (2011) Use of independent component analysis for reducing CPR artefacts in human emergency ECGs. Resuscitation 82: 79-84.

31. Amann A, Klotz A, Niederklapfer T, Kupferthaler A, Werther T, et al. (2010) Reduction of CPR artifacts in the ventricular fibrillation ECG by coherent line removal. Biomed Eng Online 9: 2.

32. Ruiz J, Irusta U, Ruiz de Gauna S, Eftestøl T (2010) Cardiopulmonary resuscitation artefact suppression using a Kalman filter and the frequency of chest compressions as the reference signal. Resuscitation 81: 1087-1094.

33. Irusta U, Ruiz J, de Gauna SR, Eftestøl T, Kramer-Johansen J (2009) A least mean-square filter for the estimation of the cardiopulmonary resuscitation artifact based on the frequency of the compressions. IEEE Trans Biomed Eng 56: 1052-1062.

34. Irusta UZ (2010) New signal processing algorithms for automated external defibrillatiors. In: University of the Basque Country, Bilbao.

35. Monsieurs KG, De Cauwer H, Wuyts FL, Bossaert LL (1998) A rule for early outcome classification of out-of-hospital cardiac arrest patients presenting with ventricular fibrillation. Resuscitation 36: 37-44.

36. Hamprecht FA, Jost D, Rüttimann M, Calamai F, Kowalski JJ (2001) Preliminary results on the prediction of countershock success with fibrillation power. Resuscitation 50: 297-299.

37. Eilevstjønn J, Kramer-Johansen J, Sunde K (2007) Shock outcome is related to prior rhythm and duration of ventricular fibrillation. Resuscitation 75: 60-67.

38. Neurauter A, Eftestøl T, Kramer-Johansen J, Abella BS, Sunde K, et al. (2007) Prediction of countershock success using single features from multiple ventricular fibrillation frequency bands and feature combinations using neural networks. Resuscitation 73: 253-263.

39. Suzuki G, Leon LJ, Kimber S, Vigmond EJ (2009) Predicting defibrillation outcome based on phase of ventricular activity during ICD implantation. Conf Proc IEEE Eng Med Biol Soc 2009: 4759-4762.

40. Endoh H, Hida S, Oohashi S, Hayashi Y, Kinoshita H, et al. (2011) Prompt prediction of successful defibrillation from 1-s ventricular fibrillation waveform in patients with out-of-hospital sudden cardiac arrest. J Anesth 25: 34-41.

41. Stewart AJ, Allen JD, Adgey AA (1992) Frequency analysis of ventricular fibrillation and resuscitation success. Q J Med 85: 761-769.

42. Goto Y, Suzuki I, Inaba H (2003) Frequency of ventricular fibrillation as predictor of one-year survival from out-of-hospital cardiac arrests. Am J Cardiol 92: 457-459.

43. Eftestøl T, Sunde K, Aase SO, Husøy JH, Steen PA (2001) “Probability of successful defibrillation” as a monitor during CPR in out-of-hospital cardiac arrested patients. Resuscitation 48: 245-254.

44. Brown CG, Dzwonczyk R (1996) Signal analysis of the human electrocardiogram during ventricular fibrillation: frequency and amplitude parameters as predictors of successful countershock. Ann Emerg Med 27: 184-188.

45. Strohmenger HU, Lindner KH, Brown CG (1997) Analysis of the ventricular fibrillation ECG signal amplitude and frequency parameters as predictors of countershock success in humans. Chest 111: 584-589.

46. Eftestol T, Sunde K, Ole Aase S, Husoy JH, Steen PA (2000) Predicting outcome of defibrillation by spectral characterization and nonparametric classification of ventricular fibrillation in patients with out-of-hospital cardiac arrest. Circulation 102: 1523-1529.

47. Gundersen K, Kvaløy JT, Kramer-Johansen J, Eftestøl T (2008) Identifying approaches to improve the accuracy of shock outcome prediction for out-of-hospital cardiac arrest. Resuscitation 76: 279-284.

48. Strohmenger HU, Lindner KH, Lurie KG, Welz A, Georgieff M (1994) Frequency of ventricular fibrillation as a predictor of defibrillation success during cardiac surgery. Anesth Analg 79: 434-438.

49. Watson JN, Addison PS, Clegg GR, Steen PA, Robertson CE (2005) Wavelet transform-based prediction of the likelihood of successful defibrillation for patients exhibiting ventricular fibrillation. Meas Sci Technol 16: L1-L6.

50. Martin DR, Brown CG, Dzwonczyk R (1991) Frequency analysis of the human and swine electrocardiogram during ventricular fibrillation. Resuscitation 22: 85-91.

51. Young C, Bisera J, Gehman S, Snyder D, Tang W, et al. (2004) Amplitude spectrum area: measuring the probability of successful defibrillation as applied to human data. Crit Care Med 32: S356-358.

52. Neurauter A, Kramer-Johansen J, Eilevstjønn J, Myklebust H, Wenzel V, et al. (2007) Estimation of the duration of ventricular fibrillation using ECG single feature analysis. Resuscitation 73: 246-252.

53. Indik JH, Peters CM, Donnerstein RL, Ott P, Kern KB, et al. (2008) Direction of signal recording affects waveform characteristics of ventricular fibrillation in humans undergoing defibrillation testing during ICD implantation. Resuscitation 78: 38-45.

54. Watson JN, Uchaipichat N, Addison PS, Clegg GR, Robertson CE, et al. (2004) Improved prediction of defibrillation success for out-of-hospital VF cardiac arrest using wavelet transform methods. Resuscitation 63: 269-275.

55. Box MS, Watson JN, Addison PS, Clegg GR, Robertson CE (2008) Shock outcome prediction before and after CPR: a comparative study of manual and automated active compression-decompression CPR. Resuscitation 78: 265-274.

56. Jalife J, Gray R (1996) Drifting vortices of electrical waves underlie ventricular fibrillation in the rabbit heart. Acta Physiol Scand 157: 123-131.

57. Panfilov AV (1998) Spiral breakup as a model of ventricular fibrillation. Chaos 8: 57-64.

58. Yu D, Small M, Harrison RG, Robertson C, Cleggb G, et al. (2000) Measuring temporal complexity of ventricular fibrillation. Physics Letters A: 68-75.

59. Callaway CW, Sherman LD, Mosesso VN Jr, Dietrich TJ, Holt E, et al. (2001) Scaling exponent predicts defibrillation success for out-of-hospital ventricular fibrillation cardiac arrest. Circulation 103: 1656-1661.

60. Podbregar M, Kovacic M, Podbregar-Mars A, Brezocnik M (2003) Predicting defibrillation success by 'genetic' programming in patients with out-of-hospital cardiac arrest. Resuscitation 57: 153-159.

61. Jagric T, Marhl M, Stajer D, Kocjancic ST, Jagric T, et al. (2007) Irregularity test for very short electrocardiogram (ECG) signals as a method for predicting a successful defibrillation in patients with ventricular fibrillation. Transl Res 149: 145-151.

62. Sherman LD, Rea TD, Waters JD, Menegazzi JJ, Callaway CW (2008) Logarithm of the absolute correlations of the ECG waveform estimates duration of ventricular fibrillation and predicts successful defibrillation. Resuscitation 78: 346-354.

63. Rodriguez E, Echeverria JC, Alvarez-Ramirez J (2009) Fractality in electrocardiographic waveforms for healthy subjects and patients with ventricular fibrillation. Chaos, Solitons and Fractals 39: 1046-1054.

64. Lin LY, Lo MT, Ko PC, Lin C, Chiang WC, et al. (2010) Detrended fluctuation analysis predicts successful defibrillation for out-of-hospital ventricular fibrillation cardiac arrest. Resuscitation 81: 297-301.

65. Jekova I (2007) Shock advisory tool: Detection of life-threatening cardiac arrhythmias and shock success prediction by means of a common parameter set. Biomed Signal Process Control 2: 25-33.

66. Koster RW, Walker RG, van Alem AP (2006) Definition of successful defibrillation. Crit Care Med 34: S423-426.

67. Shanmugasundaram M, Valles A, Kellum MJ, Ewy GA, Indik JH (2012) Analysis of amplitude spectral area and slope to predict defibrillation in out of hospital cardiac arrest due to ventricular fibrillation (VF) according to VF type: recurrent versus shock-resistant. Resuscitation 83: 1242-1247.

68. Dalzell GW, Adgey AA (1991) Determinants of successful transthoracic defibrillation and outcome in ventricular fibrillation. Br Heart J 65: 311-316.

69. Strohmenger HU, Eftestol T, Sunde K, Wenzel V, Mair M, et al. (2001) The predictive value of ventricular fibrillation electrocardiogram signal frequency and amplitude variables in patients with out-of-hospital cardiac arrest. Anesth Analg 93: 1428-1433, table of contents.

70. Jekova I, Mougeolle F, Valance A (2004) Defibrillation shock success estimation by a set of six parameters derived from the electrocardiogram. Physiol Meas 25: 1179-1188.

71. Watson JN, Addison PS, Clegg GR, Steen PA, Robertson CE (2006) Practical issues in the evaluation of methods for the prediction of shock outcome success in out-of-hospital cardiac arrest patients. Resuscitation 68: 51-59.

72. Ristagno G, Gullo A, Berlot G, Lucangelo U, Geheb E, et al. (2008) Prediction of successful defibrillation in human victims of out-of-hospital cardiac arrest: a retrospective electrocardiographic analysis. Anaesth Intensive Care 36: 46-50.

73. Neurauter A, Eftestøl T, Kramer-Johansen J, Abella BS, Wenzel V, et al. (2008) Improving countershock success prediction during cardiopulmonary resuscitation using ventricular fibrillation features from higher ECG frequency bands. Resuscitation 79: 453-459.

74. Nakagawa Y, Sato Y, Kojima T, Wakabayashi T, Morita S, et al. (2012) Electrical defibrillation outcome prediction by waveform analysis of ventricular fibrillation in cardiac arrest out of hospital patients. Tokai J Exp Clin Med 37: 1-5.

75. Callaham M, Braun O, Valentine W, Clark DM, Zegans C (1993) Prehospital cardiac arrest treated by urban first-responders: profile of patient response and prediction of outcome by ventricular fibrillation waveform. Ann Emerg Med 22: 1664-1677.

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