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ORIGINAL ARTICLE

Prompt prediction of successful defibrillation from 1-s ventricular fibrillation waveform in patients with out-of-hospital sudden cardiac arrest

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Abstracts

Purpose Ventricular fibrillation (VF) is a common cardiac arrest rhythm that can be terminated by electrical defibrillation. During cardiopulmonary resuscitation, there is a strong need for a prompt and reliable predictor of successful defibrillation because myocardial damage can result from repeated futile defibrillation attempts. Continuous wavelet transform (CWT) provides excellent time and frequency resolution of signals. The purpose of this study was to evaluate whether features based on CWT could predict successful defibrillation.

Methods VF electrocardiogram (ECG) waveforms stored in ambulance-located defibrillators were collected. Predefibrillation waveforms were divided into 1.0- or 5.12-s VF waveforms. Indices in frequency domain or nonlinear analysis were calculated on the 5.12-s waveform. Simultaneously, CWT was performed on the 1.0-s waveform, and total low-band (1–3 Hz), mid-band (3–10 Hz), and high-band (10–32 Hz) energy were calculated.

Results In 152 patients with out-of-hospital cardiac arrest, a total of 233 ECG predefibrillation recordings, consisting of 164 unsuccessful and 69 successful episodes, were analyzed. Indices of frequency domain analysis (peak frequency, centroid frequency, and amplitude spectral area), nonlinear analysis (approximate entropy and Hurst exponent, detrended fluctuation analysis), and CWT analysis (mid-band and high-band energy) were significantly different between unsuccessful and successful episodes ($P < 0.01$ for all). However, logistic regression analysis showed that centroid frequency and total mid-band energy were effective predictors ($P < 0.01$ for both).

Conclusions Energy spectrum analysis based on CWT as short as a 1.0-s VF ECG waveform enables prompt and reliable prediction of successful defibrillation.

Keywords Out-of-hospital cardiac arrest · Cardiopulmonary resuscitation · Defibrillation · Electrocardiogram · Outcome

Introduction

Ventricular fibrillation (VF) is the most common out-of-hospital cardiac arrest rhythm that can be terminated by an electrical defibrillation. Repeated futile defibrillation attempts are frequently associated with myocardial damage, resulting in reduced likelihood of survival [1, 2]. Rapid defibrillation is strongly recommended for patients with witnessed cardiac arrest as soon as a defibrillator becomes available [3]. However, performance of cardiopulmonary resuscitation (CPR) for 90 s or 3 min is recommended before attempting initial defibrillation for patients with cardiac arrest if the emergency medical service (EMS) system call-to-response interval is more than 4 or 5 min [4, 5]. Thus, the timing of defibrillation is crucial for its success. However, the exact duration of sudden-onset VF is not always clear for rescuers and, therefore, optimal timing for delivery of defibrillation may be difficult to ascertain.In addition, minimal interruption of chest

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compressions before performing defibrillation improved survival in a porcine VF model [6]. Thus, during ongoing CPR, there is a strong need for a prompt and reliable predictor of successful defibrillation.

Thus far, several predictors of successful defibrillation in VF electrocardiogram (ECG) waveform have been reported. These predictors can be generally categorized into time-domain analysis [7–9], frequency-domain analysis [8–11], nonlinear analysis of randomness and complexity [12–14], and a combination of several predictors [8, 13, 15] (Table 1). However, all such predictors require at least 3 s to determine.

Continuous wavelet transform (CWT) is one of the frequency-domain analyses. However, in contrast to Fourier transform, CWT can construct an excellent time–frequency representation of signals [16, 17]. The purpose of this study was to evaluate whether a CWT-based energy spectrum analysis on 1-s VF waveforms could reliably predict successful defibrillation as well as frequency domain or nonlinear analyses computed on 5.12-s VF waveforms immediately before delivery of electrical defibrillation.

Materials and methods

This study was approved by the Niigata prefectural medical control committee.

Patients

Adult patients (>18 years old) with sudden out-of-hospital cardiac arrest in Niigata City in Japan were resuscitated by EMS personnel or paramedics according to the American Heart Association (AHA) 2005 Guidelines for CPR & Emergency Cardiac Care between May 2006 and December 2008. Three types of biphasic defibrillators (Heart start 4000, MRxE, and FR2; Phillips, USA), with which ambulances are equipped, were used for electrical defibrillation and simultaneous online electrocardiogram (ECG) recording. The defibrillators delivered a 150-J biphasic truncated exponential wave with impedance compensation. All defibrillations were used in automated external defibrillator (AED) mode.

The self-adhesive ECG/defibrillation electrode pads were attached to the patient's skin to conform to a standard

Table 1 Human studies of prediction of successful defibrillation from ECG waveform of ventricular fibrillation

References	No. of patients	Predictor	Duration of VF waveform	AUC SENS (%), SPEC (%)
Time domain analysis				
Weaver et al. [7]	394	Peak to peak amplitude	Not reported	Not reported
Brown and Dzwonczyk [8]	55	Average amplitude	4.0 s	0.53
Strohmenger et al. [9]	26	Peak to peak amplitude	3.0 s	SENS 100, SPEC 25
Frequency domain analysis				
Stewart et al. [10]	56	Peak frequency	8.0 s	Not reported
Brown and Dzwonczyk [8]	55	Centroid frequency	4.0 s	0.72
		Peak frequency		0.70
Strohmenger et al. [9]	26	Peak frequency	3.0 s	SENS 100, SPEC 25
Young et al. [11]	46	AMSA	3.0 s	SENS 91, SPEC 94
Non-linear analysis of randomness and complexity				
Callaway et al. [12]	75	Scaling exponent	5.12 s	0.70
Prodbregar et al. [13]	47	Hurst exponent	3.0 s	Not reported
Lin et al. [14]	155	DFA	10.0 s	0.65
Combination of several predictors				
Brown and Dzwonczyk [8]	55	Peak frequency	4.0 s	SENS 100, SPEC 47
		Centroid frequency		
Eftestøl et al. [15]	156	Peak frequency	5.12 s	SENS 92, SPEC 27
		Centroid frequency		
Prodbregar et al. [13]	47	Peak to peak amplitude	3.0 s	SENS 100, SPEC 97
		Total energy of PSD		
		Hurst exponent		

ECG electrocardiogram, *VF* ventricular fibrillation, *AUC* area under curve, *SENS* sensitivity, *SPEC* specificity, *AMSA* amplitude spectral area, *DFA* detrended fluctuation analysis, *PSD* power spectrum density lead II configuration. The ECG waveform data were automatically stored in the data card of the defibrillators in digitized form (200 samples/s).

Data analysis

The data cards were collected and reviewed with a viewer software (Eventreview 3.5; Phillips, USA). Cardiac arrest with monofocal ventricular tachycardia or traumatic origin was excluded from the present study.

The 1,024 data points (=5.12 s) and the 200 data points (=1.0 s) immediately before defibrillation were selected and transformed to comma-separated value (CSV) data using a customized software (Peritec, Takasaki, Japan).

The digitized CSV data were analyzed using MATLAB ver. 7.8 (MathWorks, Natick, MA, USA). The CSV data were initially filtered through a Butterworth bandpass digital filter (0.5–32 Hz).

Successful defibrillation was defined as an organized rhythm seen at 5 s after delivery of defibrillation regardless of palpated pulsation of the common carotid artery [18]. Organized rhythm was defined as a minimum of two consecutive QRS complexes of similar morphology within a 5-s interval without background chaotic electrical activity.

All episodes in which concomitant chest compressions seemed to overlap this period were excluded.

Continuous wavelet transform (CWT)

CWT was performed using Wavelet Toolbox ver. 4.4 (MathWorks) on the 200 data points (= 1 s) of VF waveform immediately before defibrillation. The following three indices were originally developed and calculated (Fig. 1):

- Total low-band energy was defined as the sum of the energy between 1 and 3 Hz.
- Total mid-band energy was defined as the sum of the energy between 3 and 10 Hz.
- Total high-band energy was defined as the sum of the energy between 10 and 32 Hz.

Frequency analysis

Power spectrum density (PSD) was calculated using Signal Processing Toolbox ver. 4.4 (MathWorks) on the 1,024 CSV data points (= 5.12 s) of VF waveform immediately before defibrillation.

The following three indices were determined:

- Peak power frequency (Hz) was determined as the frequency with the greatest power in the PSD [8–10].
- Centroid frequency (Hz) was calculated as the weighted mean of the frequencies in PSD [8–10].
- Amplitude spectral area (AMSA) (mV Hz) was calculated as the area under the curve of amplitude frequency spectral density (ASD) [11]. ASD was calculated as the square root of PSD.

Nonlinear analysis of randomness and complexity

Nonlinear analysis was performed on the 1,024 CSV data points (= 5.12 s) of VF waveform immediately before defibrillation.

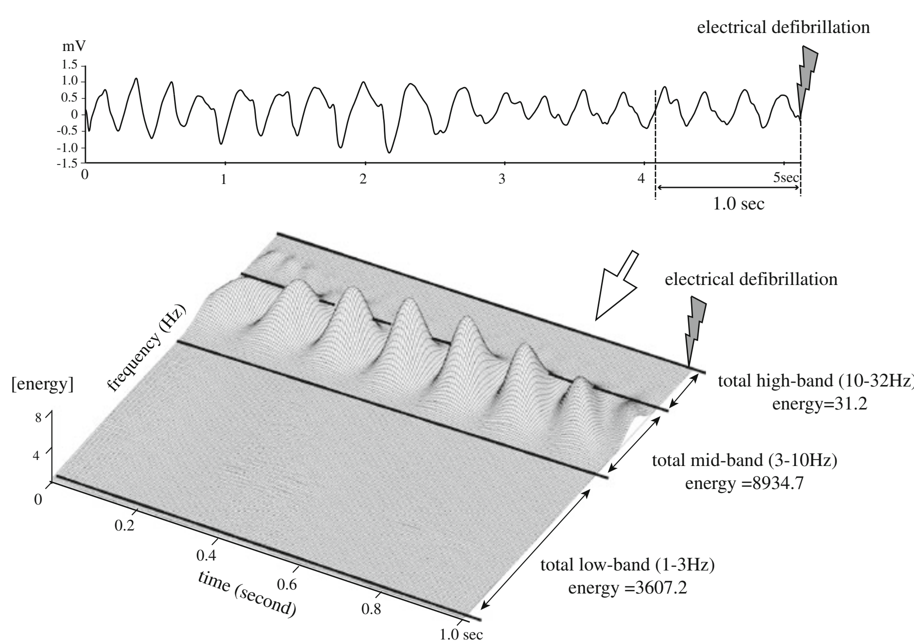

Fig. 1 Schematic illustration for energy spectrum analysis of a 1-s ventricular fibrillation electrocardiogram immediately before electrical defibrillation

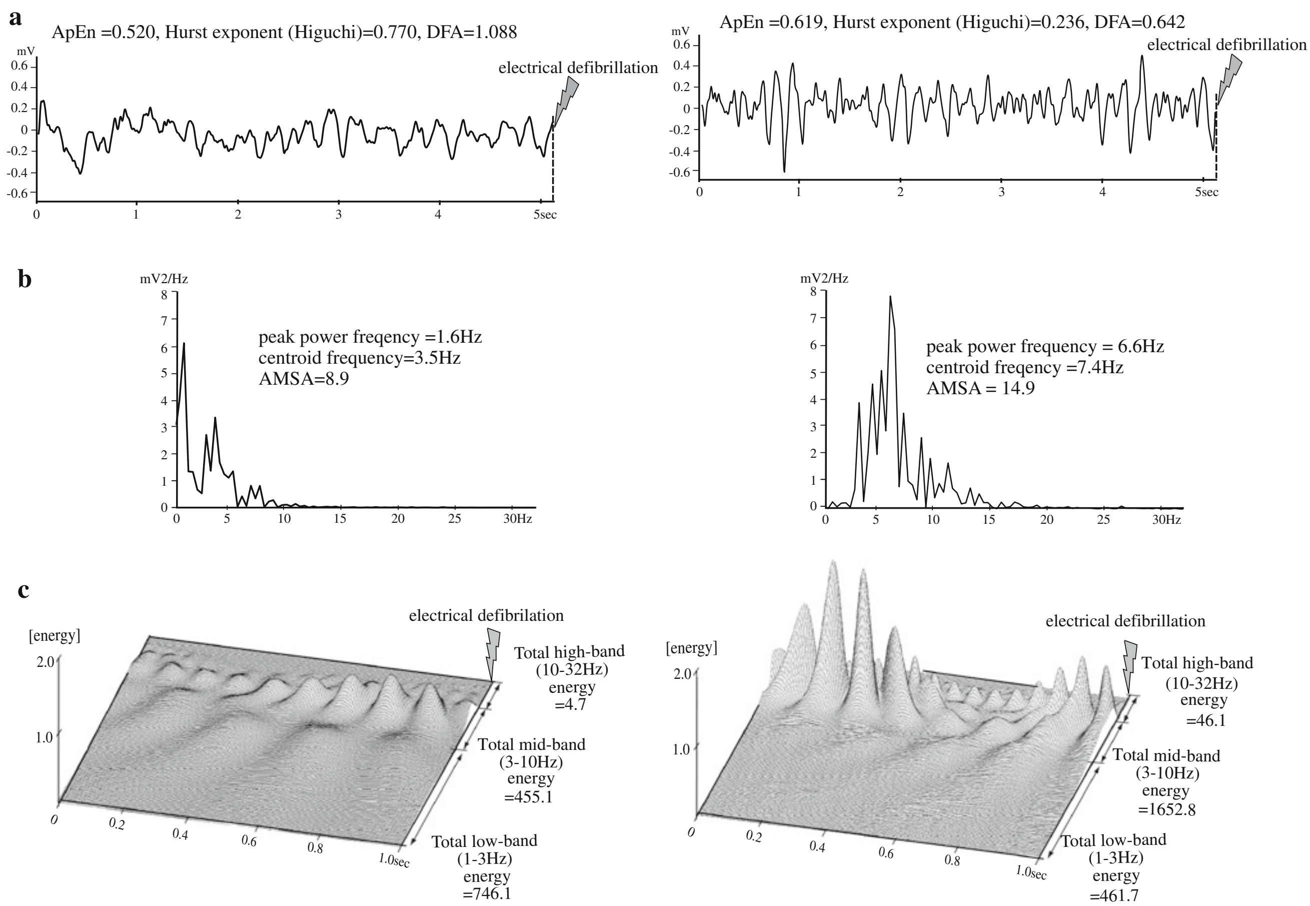

Fig. 2 Representative of unsuccessful and successful episodes. **a** Actual ventricular fibrillation electrocardiogram and computed indices of nonlinear analysis. **b** Power spectrum density and computed indices of frequency-domain analysis. **c** Energy spectrum analysis based on continuous wavelet transform performed on a 1-s ventricular fibrillation waveform immediately before defibrillation and computed band energy. Unsuccessful and successful episodes are shown in the *left* and *right panels*, respectively. *ApEn*, approximate entropy; *DFA*, detrended fluctuation analysis; *AMSA*, amplitude spectral area

The following three indices were determined:

- Approximate entropy (ApEn) generally measures randomness or unpredictability of signal [19]. A smaller value indicates simple and predictable waves, and vice versa for a larger value.
- Fractal dimension (FD) is an index for describing the irregularity of signal by measuring patterns of self-similarity [20]. A simple, regular straight-line signal has a FD approaching 1. In contrast, a complex, irregular signal has a FD approaching 2 ($1 \leq FD \leq 2$). One way to calculate FD is through the estimation of the Hurst exponent (H) [13], because H is directly related to FD: $FD = 2 - H$. In the present study, H values were estimated with the Higuchi method [21].
- Detrended fluctuation analysis (DFA) is also related to FD. A DFA value approaching 1.5 indicates a simple straight-line signal. In contrast, a DFA value approaching 0.5 indicates a complex irregular signal [22].

ApEn and DFA were computed using the MATLAB M program downloaded from the "Physio Net" Internet website (http://www.physionet.org). ApEn was computed with parameter values of $m = 2$ and $r = 0.2 \times$ standard deviation (SD) of signal. The H value was calculated by the Higuchi method using the MATLAB M program downloaded from an Internet website with a "code for the estimation of scaling exponents" (http://www.cubinlab.ee.mu.oz.au/~darryl/secondorder_cpde.html).

Statistical analysis

All statistical analyses were performed by SPSS ver. 16 (SPSS, Chicago, IL, USA). Differences of indices between unsuccessful versus successful episodes were compared using the Mann–Whitney test. Stepwise multiple logistic regression analysis was performed on the significantly different indices to evaluate significant predictors. A receiver operating characteristic (ROC) curve was plotted

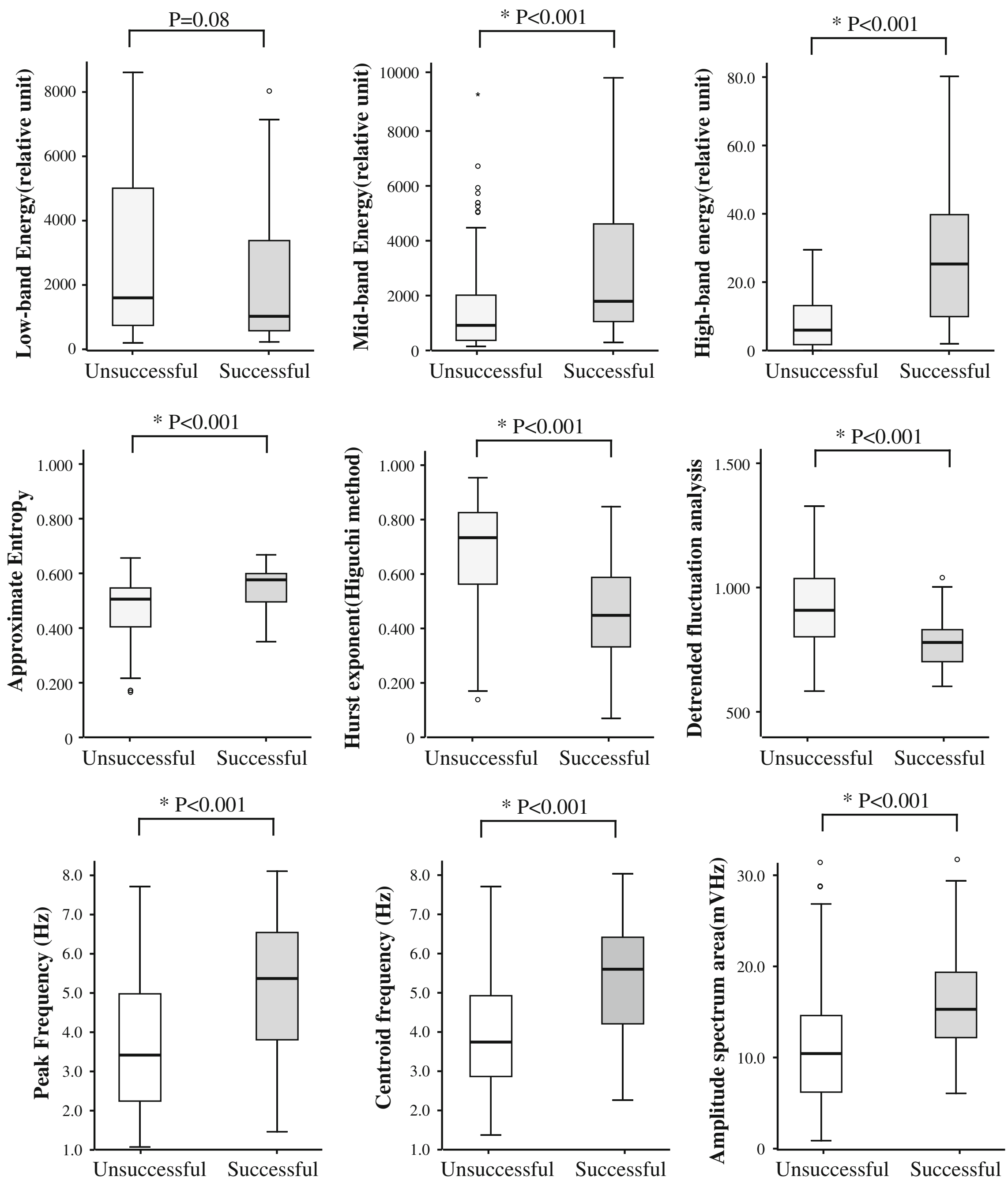

Fig. 3 *Box plots* comparing unsuccessful ($n = 164$) versus successful ($n = 69$) episodes for the nine studied indices: indices of continuous wavelet transform-based spectrum analysis, nonlinear analysis, and frequency-domain analysis are shown in the *upper*, *middle*, and *lower panels*, respectively. *Asterisk* indicates a significant difference

for the significant predictors. For all statistics, a P value $<$ 0.05 was considered significant.

Results

A total of 415 episodes of electrical defibrillation were collected from the data card of defibrillators used on 152 adult patients. Twelve episodes were removed for reasons of cardiac arrest with monofocal ventricular tachycardia, and 170 episodes were excluded because of the inability to judge successful versus unsuccessful episodes. The remaining 233 episodes, consisting of 164 unsuccessful and 69 successful episodes, were studied.

Figure 2 shows representative unsuccessful and successful episodes. Figure 3 shows a box plot of the nine studied indices comparing unsuccessful versus successful episodes. Eight indices (peak frequency, centroid

Table 2 Stepwise multiple logistic regression analysis with unsuccessful versus successful defibrillation as the dependent variable

Index	Coefficient (β)	Standard error	Wald (χ^2)	P value	Odds ratio	95% CI
Peak frequency (Hz)	−0.068	0.206	0.109	0.712	0.934	0.624–1.400
Centroid frequency (Hz)	0.800	0.133	36.2	<0.001	2.226	1.715–2.888
AMSA (mV Hz)	0.0053	0.0042	1.626	0.202	1.055	0.972–1.144
Approximate Entropy	0.554	3.719	0.022	0.881	1.741	0.01–547.378
Fractal Dimension (Higuchi)	0.132	2.861	0.002	0.963	1.14	0.004–311.896
DFA	−4.019	2.331	2.973	0.085	0.018	0–1.732
Total high-band energy (/100 relative units)	−0.268	1.199	0.050	0.823	0.765	0.073–8.015
Total mid-band energy (/100 relative units)	0.034	0.008	18.424	<0.001	1.035	1.019–1.051

AMSA amplitude spectral area, *DFA* detrended fluctuation analysis, *95% CI* 95% confidence interval for estimated odds ratio

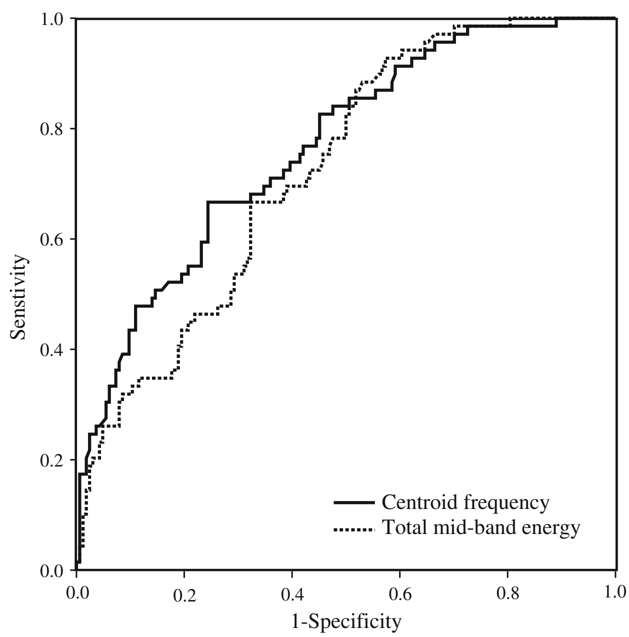

Fig. 4 Receiver operating characteristic (ROC) curves for centroid frequency and total mid-band spectrum energy

frequency, AMSA, ApEn, Hurst exponent, DFA, total high-band energy, and total mid-band energy) were significantly different ($P < 0.01$ for all).

Stepwise multiple logistic regression analysis was performed on the eight significant indices (Table 2). Of these, centroid frequency and total mid-band energy were also significant predictors ($P < 0.001$ for both). Figure 4 shows ROC curves plotted for the two predictors. The area under the curve (AUC), cutoff value, sensitivity, and specificity for the predictors are shown in Table 3.

Discussions

Predictors of successful defibrillation are generally classified into four categories: time-domain analysis [7–9], frequency-domain analysis [8–11], nonlinear analysis of randomness and complexity [12–14], and a combination of several features [8, 13, 15] (see Table 1). Predictors of time-domain analysis are basically influenced by VF ECG amplitudes. The amplitude of VF is not only dependent on the duration of VF but is also affected by several factors: recording conditions, size and position of electrodes, skin resistance, body habitus, and ventricular hypertrophy [23]. For this reason, in the present study, time-domain features were not evaluated. So far, several reliable predictors have previously been reported. However, all required 3.0- to 10-s VF waveforms for calculations (Table 1).

The main advantage of CWT is that it can elucidate spatial and temporal information simultaneously within a waveform [16, 17], which enables calculation of the energy spectrum promptly on the VF waveform. The present study shows that the total mid-band (3–10 Hz) energy for the 1-s VF waveform and centroid frequency computed using the 5.12-s VF waveform were effective predictors of successful defibrillation. To our knowledge, the total mid-band energy, which requires only a 1-s ECG waveform to compute, is the fastest predictor.

Multiple logistic regression analysis demonstrated that an increase of 1 Hz in the centroid frequency increases the possibility of successful defibrillation by 120%, and that an increase of 100 relative units in the total mid-band energy increases the possibility of defibrillation success by 3.5%. Unfortunately, % AUC for the total mid-band energy was smaller than that for the centroid frequency (0.725 vs. 0.765). However, the spectrum band classification of 1–3, 3–10, and 10–32 Hz in the present study was referred to three dominant ridges seen in CWT performed on porcine prolonged VF waveforms [24]. The distributions of frequency in VF of animals are different from humans [25]. Accordingly, further accurate prediction might be possible by changing the band classification.

Frequency-domain analysis showed that an increase of mean value of peak power frequency, centroid frequency, and AMSA were significantly associated with successful defibrillation, consistent with other prior studies [8–11, 15].

Table 3 Percent (%) AUC of ROC curve, cutoff value, sensitivity, and specificity for the two predictors

Predictors	% AUC	Standard error	95% CI	Cutoff value	Sensitivity (%)	Specificity (%)
Centroid frequency (Hz)	0.77	0.033	0.70–0.83	4.8	76.8	62.8
Total mid-band energy (/100 relative units)	0.73	0.034	0.66–0.79	12.0	66.7	61.8

AUC area under the curve, *ROC* receiver operating characteristic curve, *95% CI* 95% confidence interval for % AUC

Interestingly, peak frequency or centroid frequency in the successful defibrillation episodes was mainly aggregated in a range of 3–6 Hz, corresponding to the mid-band range (3–10 Hz) (Fig. 3 lower panel).

ApEn was designed to quantify the degree of predictability of a series of data points [19]. ApEn is fundamentally a "regularity" statistic, not a direct index of physiological complexity. Conversely, DFA and Hurst exponent measure physiological complexity [26]. In this study, ApEn, Hurst exponent (Higuchi method), and DFA were significantly different between unsuccessful versus successful episodes. A higher value of ApEn as well as a lower value of Hurst exponent or DFA occurred in the successful episodes, consistently indicating that a more irregular, unpredictable, and complex VF waveform is strongly associated with increased possibility of successful defibrillation. This finding is consistent with Amann et al. [27], who evaluated the complexity of VF waveforms with N(α) histograms in a porcine model. Recently, Lin et al. [14] have reported a significantly lower value of DFA for successful defibrillation in patients with out-of-hospital cardiac arrest.

In contrast, Callaway et al. [12] demonstrated that a lower value of scaling exponent, a measure of fractal self-similarity dimension, indicates a simpler and more regular VF waveform, suggesting early and organized VF, and leading to successful defibrillation. Similarly, Podbregar et al. [13] showed that a higher value of Hurst exponent of human VF waveform is associated with successful defibrillation. However, a higher sampling rate of 1,000 samples/s for the scaling exponent or 400 samples/s for the Hurst exponent is strongly recommended for accurate estimation in humans [28, 29]. The actual sampling rates in the studies of Callaway et al. [12] and Podbregar et al. [13] were 400 and 100 samples/s, respectively. Further studies may be required to clarify exact causes for such conflicting results.

In conclusion, CWT-based energy spectrum analysis of VF waveform can predict successful defibrillation promptly and reliably, suggesting performance of a minimal interruption of chest compressions and predefibrillation pause, which might potentially lead to more effective CPR.

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Appendix

Continuous wavelet transform (CWT)

CWT is defined as the convolution of a signal and an analyzing wavelet (ψ).

$$C(\alpha,\tau) = \sum_{t=0}^{n-1} \text{signal}\,(t)\psi * \left(\frac{t-\tau}{\alpha}\right)$$

where the asterisk indicates a complex conjugate, α indicates the scale (dilation), τ indicates a time shift, and signal (t) denotes sample t in the VF waveform segment of length n. In this study, a complex Morlet wavelet was employed as the analyzing wavelet (ψ) [16, 17].

The proportional contribution to the signal energy at a specific scale and a location τ is given by the two-dimensional wavelet energy density function:

$$E(\alpha,\tau) = \frac{[C(\alpha,\tau)]^2}{C_g}$$

where C_g is the wavelet-dependent admissibility constant that ensures conservation of energy in wavelet space [30].

Frequency-domain analysis

Fourier transform is defined as follows:

$$F(\text{fi}) = \sum_{t=0}^{n-1} \text{signal}\,(t)e^{-j2\pi \text{fi} n}$$

where fi indicates frequency and signal (t) denotes sample t in VF waveform segment of length n.

Power spectral density (PSD) describes how the power of a signal is distributed with frequency. Mathematically, it is defined as the squared modulus of the Fourier transform of the signals.

$$\text{PSD}(\text{fi}) = [F(\text{fi})]^2$$

$$\text{Peak power frequency (Hz)} = \arg\max\ \text{PSD}(\text{fi})$$

where fi indicates frequency and argmax indicates the fi attaining a max value of PSD.

$$\text{Centroid frequency (Hz)} = \frac{\sum \text{fi} \times \text{PSD(fi)}}{\sum \text{PSD(fi)}}$$

$$\text{Amplitude spectral are (AMSA) (mVHz)} = \sum \text{fi} \times \text{ASD(fi)}$$

where ASD(fi) indicates amplitude spectral density, calculated as

$$\text{ASD(fi)} = \sqrt{\text{PSD(fi)} \times \frac{\text{fi}}{2}}$$

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