Scaling Exponent Predicts Defibrillation Success for Out-of-Hospital Ventricular Fibrillation Cardiac Arrest

Clifton W. Callaway, MD, PhD; Lawrence D. Sherman, MD; Vincent N. Mosesso, Jr, MD; Thomas J. Dietrich, MD; Eric Holt, MD; M. Christopher Clarkson, MD

Background—Defibrillator shocks often fail to terminate ventricular fibrillation (VF) in out-of-hospital cardiac arrest (OOHCA), and repeated failed shocks can worsen the subsequent response to therapy. Because the VF waveform changes with increasing duration of VF, it is possible that ECG analyses could estimate the preshock likelihood of defibrillation success. This study examined whether an amplitude-independent measure of preshock VF waveform morphology predicts outcome after defibrillation.

Methods and Results—Clinical data and ECG recordings from an automated external defibrillator were obtained for 75 subjects with OOHCA in a suburban community with police first responders and a paramedic-based emergency medical system. An estimate of the fractal self-similarity dimension, the scaling exponent, was calculated off-line for the VF waveform preceding shocks. Success of the first shock was determined from the recordings. Return of pulses and survival were determined by chart review. The first shock resulted in an organized rhythm in 43% of cases, and 17% of cases survived to hospital discharge. A lower mean value of the scaling exponent was observed for cases in which the first defibrillation resulted in an organized rhythm (P=0.004), for cases with return of pulses (P=0.049), and for cases surviving to hospital discharge (P<0.001). Receiver operator curves revealed the utility of the scaling exponent for predicting the probability of restoring an organized rhythm (area under the curve=0.70) and of survival (area under the curve=0.84).

Conclusions—The VF waveform in OOHCA can be quantified with the scaling exponent, which predicts the probability of first-shock defibrillation and survival to hospital discharge. (Circulation. 2001;103:1656-1661.)

Key Words: fibrillation ■ heart arrest ■ defibrillation ■ electrocardiography ■ survival
scaling dimension increases over time, we hypothesized that a lower scaling dimension in the initial VF waveform would be correlated with successful defibrillation.

Methods
This study was approved by the Institutional Review Board of the University of Pittsburgh. Police in 7 suburban municipalities with a total population of 145,000 were provided with Lifepak 300 semiautomated defibrillators (Physio-Control Inc). In each community, police arrive at medical emergencies before paramedics in ~50% of cases. Data were collected between February 1, 1992, and January 30, 1998. Police training and data collection methods were detailed previously. Subjects were adult patients (>18 years old) with nontraumatic cardiac arrest for whom an initial rhythm of VF was recorded by the AED. For each patient, the recording leads/defibrillation pads (FAST-PATCH, Physio-Control Inc) of the AED were applied to the chest. The ECG waveform was recorded on analog tapes along with an audio record. After each AED use, tapes and clinical information were collected by the investigators. All available ECG recordings were included.

Analysis of the ECG recording was conducted off-line. The ECG waveform was digitized at 400 samples per second from analog tape recordings by a PC-compatible computer and analog/digital converter (PowerLab, AD Instruments). The resulting digital records were analyzed with the Chart software package (AD Instruments) as well as customized software written in C. After selecting the epoch, all calculations were performed entirely by the computer.

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Figure 1. Calculation of scaling exponent as estimate of fractal self-similarity dimension. Traces are shown of AED-recorded ECG from subjects with successful (A, B) and failed (C, D) shocks. Illustrated cases exhibited median values for scaling exponent in successful (A) and failed (B) shock groups. Sum of absolute potential differences [L(k)] between sampling points of VF waveform are plotted against lag (k) on log-log axes (A and D). Slope of resulting plot is calculated at inflection point of this curve; scaling exponent is defined as (1-slope). In these examples, successful defibrillation resulted for case (A, B) in which slope was −0.237 (scaling exponent=1.237), whereas failed defibrillation resulted for case (C, D) in which slope was −0.323 (scaling exponent=1.323).

\[ L(k) = \frac{2048}{k} \sum_{i=1}^{2048-k} |X(i) - X(i+k)| \]

The resulting values of L(k) were fitted to an exponential function describing the scaling relation between L(k) and the lag k.

\[ L(k) = k^{(1-d)} \]

This function described a curve with a consistent plateau in the region centered between k=5 and k=20. To standardize the estimation of the scaling region, the inflection point of the log-log plot of L(k) versus k was determined by the computer by calculating the local slope of the curve for 5 point regions centered around each point and identifying the maximum. The slope of a least-squares line was fitted to the log-log plot of L(k) versus k, with 10 points centered around the inflection point. The scaling exponent d was calculated as d=1−slope (Figure 1).

The scaling exponent was compared between cases with successful or failed shocks. Successful shocks were defined as cases in which VF was converted to an organized rhythm that was sustained for ≥30 seconds with or without a pulse. Failed shocks either resulted in continued VF or asystole (unorganized rhythms). Although asystole is considered a successful defibrillation from an electrophysiological standpoint, defining success as restoration of an organized postshock rhythm is more relevant to clinical outcome. Preliminary analyses indicated that the scaling measures did not differ between subjects with postshock asystole and subjects with persistent VF. Other outcome measures included the return of a spontaneous circulation (ROSC) at any time during the resuscitation, survival to hospital admission, and survival to hospital discharge.
Characteristics of Study Population

<table>
<thead>
<tr>
<th>Response to First Defibrillation</th>
<th>Organized Rhythm (Success)</th>
<th>VF or Asystole (Failure)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>31</td>
<td>44</td>
</tr>
<tr>
<td>Age, y</td>
<td>60.6±15.5</td>
<td>66.7±12.0</td>
</tr>
<tr>
<td>Sex, % men</td>
<td>74.2%</td>
<td>75.0%</td>
</tr>
<tr>
<td>Witnessed, %</td>
<td>74.2%</td>
<td>73.8%</td>
</tr>
<tr>
<td>Bystander CPR, %</td>
<td>45.2%</td>
<td>34.1%</td>
</tr>
<tr>
<td>Call received to paramedic arrival, min</td>
<td>6.0±2.5</td>
<td>7.1±2.9</td>
</tr>
<tr>
<td>Call received to defibrillation, min</td>
<td>5.9±1.9</td>
<td>6.7±2.3</td>
</tr>
<tr>
<td>ROSC, %</td>
<td>64.5%</td>
<td>43.2%</td>
</tr>
<tr>
<td>Survival to hospital admission, %</td>
<td>41.4%</td>
<td>23.1%</td>
</tr>
<tr>
<td>Survival to hospital discharge, %</td>
<td>29.0%</td>
<td>9.1%</td>
</tr>
</tbody>
</table>

The mean scaling exponent was compared between cases with different clinical outcomes by use of the t test. The proportions of subjects with good clinical outcomes were compared for different ranges of the scaling exponent by means of the χ² analysis. Associations between dichotomous categorical variables and continuous variables were examined by means of the t test. Multiple linear regression was used to determine the association between the scaling exponent and other continuous variables. Stepwise logistic regression was performed to evaluate candidate variables (age, sex, time from call received until shock, absence or presence of bystander CPR, whether collapse was witnessed or unwitnessed, and value of the scaling exponent) as predictors of the probability of successful defibrillation by the first shock (SPSS-PC, SPSS Inc.). Shock success was expressed as a binary variable. At each step, the candidate predictor variable with the highest association with the dependent variable was introduced into the model, and variable entry was halted when the resulting improvement in the fit of the model was not significant. Identical regression was performed to identify contributing variables that predict the likelihood of ROSC, admission to the hospital, or discharge from the hospital. For all statistics, the criterion for significance was a level of P<0.05.

**Results**

AED recordings were obtained from 75 cases of VF cardiac arrest in which defibrillation was attempted before other advanced life support. During the study interval, the community Emergency Medical Systems responded to 649 cases of cardiac arrest, and VF was the initial rhythm in 222 cases. Police first responders applied an AED and attempted defibrillation in 89 cases. The 75 cases used for this analysis represent all cases for which ECG recordings were successfully retrieved from the AED.

The first shock by the AED successfully converted VF into an organized rhythm in 31 cases (41.3%). Successful defibrillation by the first AED shock was associated with ROSC during the resuscitation (Table, χ²=4.05, df=1, P=0.044). Although more of the subjects with successful AED defibrillation were admitted to the hospital, this difference was not significant. The proportion of subjects discharged alive from the hospital was higher after successful AED defibrillation (Table, χ²=5.05, df=1, P=0.025). Age, sex ratio, proportion in which collapse was witnessed, proportion with bystander CPR, and delay from receiving call to delivery of shock did not differ between groups with successful and failed shocks (Table).

Analysis of the VF waveform confirmed that a scaling relation existed between the lag, k, and the sum of potential changes, L(k). The region of scaling was consistently observed for values of log(k) between 0.6 and 1.2, corresponding to sampling frequencies between 25 and 100 Hz. The least-squares line fitted by computer to this scaling region had high correlation coefficients (range, 0.967 to 0.999). The value of the scaling exponent ranged from 1.11 to 2.00.

Mean values for the scaling exponent were lower for groups with better clinical outcomes (Figure 2). The scaling exponent differed between cases with successful first shocks and those with failed first shocks (t=2.94, df=73, P=0.004), between cases with ROSC and with no ROSC (t=2.79, df=68.85, P=0.049), and between cases with survival to hospital discharge and with no survival (t=5.26, df=60.97, P<0.001). There was a trend toward lower scaling exponents in cases with survival to hospital admission compared with cases pronounced dead in the emergency department (t=1.02, df=66, P=0.059).

Lower values of the scaling exponent were associated with an increased probability of successful defibrillation (Figure 3). The proportion of subjects successfully defibrillated by the AED was highest (73%) when the initial scaling exponent was in the range of 1.00 to 1.19 (χ²=11.31, df=4, P=0.023). Furthermore, the value of the scaling exponent was related to the proportion of subjects who had ROSC (χ²=11.16, df=4, P=0.025), who survived to hospital admission (χ²=11.23, df=4, P=0.024), and who survived to hospital discharge (χ²=17.57, df=4, P=0.0015).

Stepwise logistic regression identified the scaling exponent and age as the only variables associated with first-shock defibrillation success. Including other variables listed in the Table did not significantly improve the resulting model. Coefficient estimates (±SE) were 4.36±1.67 for scaling exponent and 0.046±0.022 for age. Logistic regression identified the scaling exponent as the only variable associated with ROSC, admission to the hospital, and survival to hospital discharge. To confirm the incremental value of VF
waveform analysis for predicting defibrillation success, a stepwise logistic regression model was examined in which all other candidate variables (age, sex, witnessed, bystander CPR, time from call receipt to paramedic arrival, and time from call receipt to shock) were forced into the model in the first step. The scaling exponent was then added in the second step, resulting in a significant improvement in the $-2\log$ likelihood of the model ($\text{improvement}=6.10$, $df=5$, $P=0.0135$). Because amplitude and scaling exponent covaried, there was no incremental benefit of scaling exponent when amplitude was included in the model.

Receiver operator curves (ROC) were constructed to describe the utility of the scaling exponent by itself for predicting defibrillation by the first shock, ROSC, or discharge from the hospital (Figure 4). Areas under these curves were 0.70, 0.71, and 0.84, respectively. For comparison, the centroid frequency and root-mean-square amplitude were calculated from the same segments of VF. Centroid frequency was correlated with scaling exponent ($R^2=0.204$, $F[1,73]=18.7$, $P<0.001$). Areas under the ROC curve describing the utility of centroid frequency for predicting defibrillation by the first shock, ROSC, or discharge from the hospital were 0.53, 0.53, and 0.51, respectively. Root-mean-square amplitude also was related to the scaling exponent. A semilogarithmic relation between these variables provided the best fit ($R^2=0.788$, $F[1,73]=271.5$, $P<0.001$). Consistent with the close relation between amplitude and scaling exponent, the areas under the ROC graphs indicated that amplitude could predict defibrillation success, ROSC, and discharge from the hospital. Areas under these curves were 0.75, 0.71, and 0.84, respectively.

Several factors may influence the value of the scaling exponent. Among continuous variables, the time from call...
measured in human VF during OOHCA and that it has similar magnitude and behavior in humans and swine.12,13

Significant improvements are needed for treatment of OOHCA. In one series, shocks failed to terminate VF or resulted in asystole 75% of the time.20 Many previous studies have noted that repeated unsuccessful defibrillation attempts can increase myocardial damage and dysfunction as well as increase energy requirements for subsequent defibrillation.21 Furthermore, postshock ST-segment displacement increases with increasing energy delivered and is believed to increase with multiple shocks.22 These data emphasize the need to improve the likelihood of successful defibrillation by the first delivered shock in OOHCA.

Although decreasing the interval from collapse to shock can increase resuscitation success,5 alternative strategies may improve outcomes for the remainder of patients with prolonged VF. Studies in animals have provided evidence that reperfusion and reoxygenation of the fibrillating heart increase the probability of achieving organized electrical activity after shock.19,25,26 Likewise, introducing a 90-second period of CPR before attempting defibrillation improves survival in humans.6 This beneficial effect of antecedent CPR affects predominantly those cases in which the delay before arrival of therapy exceeded 4 minutes.

Development of a tool for stratifying patients according to their probability of responding to standard treatment could allow application of these alternative algorithms without delaying defibrillation for patients in whom it is likely to succeed. In particular, the scaling exponent described here may be a correlate of the elapsed ischemic interval before attempting defibrillation (Figure 5). Although the sensitivity of this measure for identifying cases for which defibrillation will succeed may not justify withholding shocks altogether, prior knowledge of the probability of shock success could help guide the timing or energy of electrical therapy. For example, subjects with prolonged VF and high scaling exponents may benefit from brief periods of artificial perfusion before electrical therapy.6

Prior studies used quantitative measures of the VF waveform morphology to estimate the duration of VF and its likelihood of successful defibrillation.7–10 For example, centroid frequency, a measure based on spectral analysis, varies with the duration of VF.11 Use of centroid frequency is limited by its multiphasic change with time. Because of this multiphasic profile, a particular value of the centroid frequency is not uniquely associated with a particular duration of VF. Other studies have found that the amplitude of the VF waveform can predict successful defibrillation.7,8 However, amplitude measurements can be affected by electrode configuration, placement, body habitus, impedance, and recording equipment.

Nonlinear dynamic measures, such as the fractal dimension, are more appropriate for quantifying nonperiodic waveforms such as VF. Complex dynamic behavior has been described in several models of VF.27,28 Furthermore, measurements based on nonlinear dynamics have previously been developed for the VF waveform in stabilized animal preparations.29 In humans and in unperfused animals, the VF waveform does not exhibit true fractal structure because it has scaling relations and self-similarity only over a limited range of time scales (Figure 1).30

**Figure 5.** Scaling exponent increases with duration of VF. Scaling exponent is plotted versus time from call receipt to shock for cases of witnessed collapse. Regression lines for cases with no bystander CPR and for cases with bystander CPR (excluding 1 outlier at 8 minutes) are illustrated.

The scaling exponent was lower in cases with unwitnessed arrest (1.46 ± 0.28, n = 21) (t = 2.10, df = 26.83, P = 0.045). The value of the scaling exponent did not differ between men and women or between cases with or those without bystander CPR.

The scaling exponent increased with duration of untreated VF (Figure 5). In witnessed arrests (n = 45), in which the time of emergency call receipt is a valid surrogate for the time of onset of VF, the interval from call receipt until first shock was positively correlated with scaling exponent (R² = 0.197, F[1, 61] = 15.01, P = 0.001). Age was not associated with the value of the scaling exponent. The scaling exponent was lower in cases with witnessed arrest (1.32 ± 0.18, n = 54) than in cases with unwitnessed arrest (1.46 ± 0.28, n = 21) (t = 2.10, df = 26.83, P = 0.045). The value of the scaling exponent did not differ between men and women or between cases with or without bystander CPR.

The scaling exponent increases with duration of untreated VF because it has scaling relations and self-similarity only over a limited range of time scales (Figure 1)30

**Discussion**

These data illustrate the use of a measure derived from fractal geometry for quantifying the VF waveform and predicting response to shocks. This measure, the scaling exponent, estimates the self-similarity dimension of the waveform.14 The scaling exponent provides a measure that is independent of the absolute amplitude of the recorded signal. Thus, the scaling exponent can be compared between recordings made with different equipment and different electrodes. For example, the present data confirm that the scaling exponent can be measured in human VF during OOHCA and that it has similar magnitude and behavior in humans and swine.12,13

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and because it is not stationary over time. Nevertheless, measures of fractal dimension over limited ranges have proven useful for characterizing many natural phenomena. Although amplitude and scaling exponent are correlated in this data set, the calculated value of the scaling exponent does not depend on the absolute amplitude of the waveform. Thus, this measure can be compared between different recording conditions and even between different studies.

The present data suggest that the structure of the human VF waveform evolves over time (Figure 5). A similar increase in the scaling exponent over time has been reported in swine. Conceptually, the scaling exponent distinguishes coarse VF (low scaling exponent) from fine VF (high scaling exponent). An alternative interpretation is that low values of the scaling exponent reflect more large-scale structure in the VF waveform, whereas high values of the scaling exponent reflect less large-scale structure. Previous investigations in dogs suggest that stronger correlations between the time of depolarization in spatially separated parts of the myocardium are associated with a greater likelihood of successful defibrillation. Furthermore, the correlation between electrical depolarization in spatially separated pieces of myocardium decreases over time. It is possible that the scaling exponent is a macroscopic measure of the spatial and temporal correlation of myocardial depolarization. Consequently, lower scaling exponents are associated with a greater likelihood of successful defibrillation (Figures 2 and 3). Taken together, these data suggest that analyses of VF waveforms provide some insight into the physiological state of the subject, which is perhaps related to the total duration of ischemia.

Summary
Human VF exhibits a time-dependent structure that can be quantified by the amplitude-independent fractal self-similarity dimension. This scaling exponent is an estimate of the fractal dimension. Over time, the scaling exponent increases, reflecting a loss of structure in the VF waveform. Moreover, the absolute value of the scaling exponent predicts the likelihood of successful defibrillation and ultimate survival. Even with consideration of other potential factors that may influence resuscitation, this tool remains predictive and may have utility in guiding future therapeutic trials.

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References
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