SUPPLEMENTAL MATERIAL
Data S1.

Supplemental Methods 1. Calculation of VF-waveform characteristics

Data pre-processing

Each ventricular fibrillation (VF) signal was sampled at a sampling frequency of $f_s = 1000$ Hz. The characteristics were determined from the time segment of 4.1 seconds prior to the first shock delivery. Each segment was pre-processed with a fourth-order Butterworth bandpass filter with cut-off frequencies of 1 and 48 Hz. To cancel phase shift the filter was applied once forward and once backward in time, which is what the Matlab command `filtfilt` does, resulting in the filtered VF-segment $x_n$, for which $n \in \{1, 2, \ldots, N\}$ with number of samples of $N = 4096$.

Time domain parameters

- The mean absolute amplitude (mV) is computed as the mean of all absolute samples of the filtered time segment, following:

\[
MAA = \frac{1}{N} \sum_{i=1}^{N} |x_i|
\]

- The median slope (mVs$^{-1}$) is calculated by taking the median of all sample-to-sample differences in the signal, following:

\[
MDS = \text{median}(|x_i - x_{i-1}| \cdot f_s)
\]

for samples $2 \leq i \leq 4096$.

Frequency domain parameters

A standard Fast Fourier Transform (FFT) of the VF segment returns $N$ Fourier coefficients $\hat{x}_1, \hat{x}_2, \ldots, \hat{x}_N$. Only the first $N/2$ coefficients are relevant and they correspond to the $N/2$ frequencies $f_k = k \cdot f_s/N$ with $k \in \{0, 1, \ldots, N/2\}$. 
- The amplitude spectrum area (mVHz) is defined as

\[ AMSA = \frac{2}{N} \sum_{k=0}^{N/2} |\hat{x}_k \cdot f_k|, \]

but in this sum only those indices \( k \) are taken into account for which \( 2 \leq f_k \leq 48 \).

The power spectrum of the VF signal, also called the power spectral density, describes the power present in the signal as a function of the frequency, per unit frequency. It is defined as

\[ PSD_k = \beta_k |\hat{x}_k|^2, \]

with \( k \in \{0, 1, ..., N/2\} \) and \( \beta_k = \begin{cases} \frac{2}{f_s N} & k \in \{1, 2, ..., \frac{N}{2} - 1\} \\ \frac{1}{f_s N} & k = 0 \text{ or } k = N/2 \end{cases} \)

- From the power spectrum, the power spectrum area (mV^2Hz) was calculated as:

\[ PSA = \frac{f_s}{N} \sum_{k=0}^{N/2} |PSD_k \cdot f_k| \]

- The dominant frequency (Hz) is defined as the frequency \( f_k \) for which \( PSD_k \) attains its maximum:

\[ DF = \text{arg max}_{f_k} PSD_k \]

- The median frequency (Hz) is computed as the smallest frequency \( f_k \) for which the trapezoidal integral approximation \( \left( \sum_{i=0}^{k} |\hat{x}_i|^2 \right) - (|\hat{x}_0|^2 + |\hat{x}_k|^2)/2 \) is at least 50% of the total trapezoidal \( \left( \sum_{i=0}^{N/2} |\hat{x}_i|^2 \right) - (|\hat{x}_0|^2 + |\hat{x}_{N/2}|^2)/2 \). Likewise, we compute the 25% and 75% frequencies and then the bandwidth (Hz) is defined as the difference between these two frequencies.
**Measures of signal organization**

**Organization index**

First, the bandwidth of the fundamental peak (corresponding to the dominant frequency) was obtained, given by a 75% amplitude decrease. Subsequently, harmonic peaks corresponding to the DF were assessed, as well as the bandwidth of these harmonic peaks.

- The organization index was defined as the ratio between the summed power of the bandwidth of the fundamental and its harmonic peaks, and the total power (Figure S1).

**Detrended fluctuation analysis**

Detrended fluctuation analysis (DFA) gives information about the complexity of the VF morphology. DFA-measures are computed following standardized steps, which is visualized in Figure S2.

Correction for the offset of the original time series by subtracting the mean of the signal (1); The resulting signal is subsequently integrated by taking the cumulative sum of the signal (2); This signal is divided in boxes of equal sample length \( n \), with \( n \in \{2^1, 2^2 \ldots 2^{12} = 4096\} \). In each box, the local linear trend is calculated (3) and subtracted from the integrated time series (4). From these detrended signals, the root mean square (RMS) is calculated, representing the fluctuation \( F \) in that specific box size. This process is repeated for all values of \( n \); (5) the relationship between \( F(n) \) and \( n \) is plotted on logarithmic axes. The DFA scaling exponent \( \alpha \) is the slope of the trend line of this function, estimated using linear regression.

In the current study, we report on two DFA scaling exponents (Figure S3):

- **\( DFA\alpha_1 \)**: defined as the DFA scaling exponent on small time scales, i.e. 0.004 to 0.128 seconds.
- **\( DFA\alpha_2 \)**: defined as the DFA scaling exponent on larger time scales, i.e. 0.128 to 4.0 seconds.
Data S2. Support vector machine

Support vector machine (SVM) is a machine learning technique which enables discrimination between two classes by an algorithm that maximizes the distance between these classes, using a prespecified amount of input features. The mathematical function that gives the optimal separation between the classes is called the hyperplane, which allows for discrimination between the two classes. SVMs have been used in multiple VF-studies to combine VF-waveform characteristics and predict defibrillation success and clinical outcome measures. [5,6]

Settings of SVM-models in this study

In the current study, the function fitcsvm in Matlab (version 2018a, The Mathworks, Natick, USA) was used for training and validation of the SVM-models. In these preliminary analyses to investigate the concept of machine learning for MI-identification, fixed settings were used for model optimization. Models were trained using normalized input features (mean = 0, standard deviation = 1). Optimization of the regularization parameter $C$ was performed by varying this parameter following:

$C = 2^{-7}, 2^{-6} \ldots 2^7$ and taking the value with the maximum AUC (Figure S4). For all models, a linear kernel was used, with automatic scaling of the kernel. Five-fold cross validation was performed using the crossval function in Matlab. The process of data analysis is visualized in Figure S5.

Data flowchart and input features

The input feature matrix consists of $N \times M$ elements, with $N$ the number of patients and $M$ the number of input features. $M$ is determined by the number of leads (either a single lead of 12-leads) and the number of VF-characteristics per lead (either a single lead or the entire set of 10 VF-characteristics). In case of a 12-lead approach, the difference with V1 was calculated for each VF-characteristic as well. Hence, $M$ differed for all three SVM-approaches that were used:
(A) Single lead II, 10 VF-waveform characteristics (1 lead x 10 VF-characteristics = 10 input features per patient

(B) 12 leads, single VF-characteristics (12 leads x 1 VF-characteristic + 11 x 1 difference with V1 = 23 input features

(C) 12 leads, 10 VF-characteristics (12 leads x 10 VF-characteristic + 11 x 10 difference with V1 = 230 input features
Table S1. Individual VF-characteristics and discriminative performances, single lead II.

| VF-characteristic | All patients N=206 | MI+ | MI- | P-value comparison | C-statistic |
|-------------------|--------------------|-----|-----|--------------------|-------------|
| AMSA              | 11.3 (9.1-16.1)    | 10.7 (8.7-13.4) | 12.7 (9.7-17.7) | 0.006 | 0.613 (0.535-0.692) |
| BW                | .49 (.49-.73)      | .49 (.49-.98)   | .49 (.24-.73)   | 0.06  | 0.576 (0.498-0.653)  |
| DFA1              | 1.97 (1.95-1.98)   | 1.96 (1.95-1.98) | 1.97 (1.96-1.98) | 0.07  | 0.574 (0.496-0.652)  |
| DFA2              | .26 (.22-.31)      | .27 (.23-.31)   | .25 (.21-.30)   | 0.11  | 0.565 (0.485-0.646)  |
| DF                | 5.1 (4.9-5.6)      | 5.1 (4.9-5.6)   | 5.4 (4.9-5.9)   | 0.11  | 0.566 (0.486-0.650)  |
| MAA               | .15 (.11-.24)      | .14 (.10-.21)   | .19 (.12-.27)   | 0.003 | 0.619 (0.541-0.697)  |
| MDF               | 5.4 (4.9-5.6)      | 5.1 (4.9-5.6)   | 5.4 (4.9-5.9)   | 0.08  | 0.570 (0.491-0.649)  |
| MDS               | 4.6 (3.5-7.1)      | 4.2 (3.2-5.7)   | 6.1 (3.8-8.0)   | 0.001 | 0.631 (0.553-0.709)  |
| OI                | .70 (.56-.78)      | .68 (.51-.77)   | .72 (.60-.79)   | 0.04  | 0.586 (0.508-0.664)  |
| PSA               | .18 (.10-.42)      | .17 (.08-.27)   | .26 (.12-.58)   | 0.001 | 0.625 (0.558-0.713)  |

§ Statistically not different from the C-statistic of AMSA (De Long method p>0.006 after Bonferroni correction)
Table S2. Performances and characteristics of SVM-models with combined VF-characteristics.

| SVM-model | C-statistic       | Optimal regularization parameter C |
|-----------|-------------------|-----------------------------------|
| Lead II   | 0.66 (0.59-0.73)  | $2^3$                             |
| 12 leads  | 0.74 (0.67-0.80)  | $2^{-2}$                          |
Table S3. Individual characteristics and model performances, 12-lead SVM-models.

| SVM-model | C-statistic               | Optimal regularization parameter C |
|-----------|---------------------------|-----------------------------------|
| AMSA, 12-leads | 0.744 (0.678-0.803) | 2^3                               |
| BW, 12-leads   | 0.603 (0.531-0.671)^*  | 2^5                               |
| DFA1, 12-leads | 0.600 (0.528-0.668)^7   | 2^4                               |
| DFA2, 12-leads | 0.545 (0.474-0.616)^†   | 2^4                               |
| DF, 12-leads    | 0.634 (0.563-0.701)^§    | 2^5                               |
| MAA, 12-leads   | 0.721 (0.654-0.782)^§    | 2^3                               |
| MDF, 12-leads   | 0.615 (0.544-0.683)^§    | 2^7                               |
| MDS, 12-leads   | 0.727 (0.659-0.787)^§    | 2^1                               |
| OI, 12-leads    | 0.641 (0.570-0.707)^§    | 2^3                               |
| PSA, 12-leads   | 0.743 (0.677-0.802)^§    | 2^2                               |

* Inferior to C-statistic of AMSA model (DeLong method p<0.006 after Bonferroni correction)

§ Statistically not different from the C-statistic of AMSA model
Figure S1. Representation of the organization index. The organization index was calculated as the ratio between the summed power of the bandwidth of the fundamental and its harmonic peaks, and the total power.
Figure S2. Stepwise process of detrended fluctuation analysis.
Figure S3. Two scaling exponents of detrended fluctuation analysis (DFA$\alpha_1$ and DFA$\alpha_2$). The red lines represent the scaling exponents as obtained from the DFA analysis. DFA$\alpha_1$ is defined as the DFA scaling exponent on small time scales, i.e. 0.004 to 0.128 seconds; DFA$\alpha_2$ is defined as the DFA scaling exponent on larger time scales, i.e. 0.128 to 4.0 seconds.
Figure S4. Optimization of the regularization parameter $C$ of the support vector machine models. Overview of the obtained C-statistics for all chosen values of the regularization parameter $C$. The red dot represents the optimal value of $C$ per VF-characteristic.
Figure S5. Flowchart of the support vector machine process.
Figure S6. Ancillary analysis on infarct localization. ROC curves of anterior vs inferior myocardial infarction, all VF characteristics combined in a single lead (blue, C= 2-6) or multiple lead (red, C=20) SVM model.

|                | Lead II model | 12-lead model | p-value (DeLong method) |
|----------------|---------------|---------------|-------------------------|
| ROC analysis   | 0.767 (0.671-0.847) | 0.888 (0.809-0.943) | 0.0096                  |
| PPV*           | 74%           | 83%           |                         |

* to identify an inferior MI