In-hospital and long term neurological outcome prognostication using an algorithm based on the analysis of ventricular fibrillation from the EKG of patients with sudden cardiac death (AWAKE)

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Background: Sudden cardiac death (SCD) is a leading cause of mortality and carries a dismal neurological outcome (NO) among patients admitted alive to acute cardiac care units (ACCU). A big share of SCD are found in ventricular fibrillation (VF). VF waveform is dynamic and it can be characterized by spectral analysis at the very time of ACCU admission.

Purpose: To validate in a multicenter cohort an algorithm based on spectral variables of VF waveform to early predict neurological outcome at hospital discharge and follow-up, and to compare its performance with currently established prognostic tools.

Methods: Multicenter study in which 5 hospitals recruited patients, resuscitated from SCD due to VF whose EKG was available, and admitted to ACCU with expertise in SCD. EKG tracings were scanned and analyzed with a custom MATLAB script delivering spectral variables to be entered in an algorithm to predict NO. NO was assessed by Cerebral Performance Category (CPC) during admission and after a minimum 6-month follow-up period. The primary endpoint was favorable neurological outcome (FNO, defined as CPC 1 and 2) during hospital admission, and the secondary endpoint was FNO at long-term follow-up. Statistical data were analyzed with SPSS and EPIDAT.

Results: We included 168 patients out of 678 screened in participant hospitals among admissions from 2007 to 2022. The main cause of exclusion was a rhythm different from VF at the time of medical assistance (n=329, 48%) or VF EKG unavailable (n=151, 22%). Ninety-five patients (57%) were admitted in comatose status (Glasgow <9). Baseline characteristics are depicted in Picture 1.

FNO during admission was documented in 136 patients (81%). Twenty-nine patients (17%) died during hospitalization. A spectral-based model using VF tracings early predicted FNO with an area under the curve (AUC) value of 0.85 (CI95% 0.77-0.93). There was overlap with the predictive performance obtained with the peak value of neuron-specific enolase (NSE) (0.85; CI95% 0.74-0.95) (Picture 2, A). Other prognostic tools showed similar or lower diagnostic yield and results were obtained at a later time after admission (Picture 2, B,D).

Long-term follow-up was obtained for 166 cases (2 foreign patients were impossible to retrieve). Patients discharged alive were followed for 17 (± standard deviation 21) months. FNO was present in 136 (82%). The spectral-based model predicted FNO with AUC 0.83 (CI95% 0.74-0.92), similar to NSE (AUC 0.87, CI95% 0.77-0.97) (Picture 2, C). Other tools performed in follow-up similar to during admission (Picture 2, D).

CONCLUSION: A model based on VF spectral analysis predicts neurological outcome after SCD with an accuracy similar to current validated tools, but with no requirement for drug withdrawal or waiting period in comatose patients. This model estimates outcomes at the earliest moment of hospital admission and its predictions remain valid in the long run.
Baseline characteristics

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>N=168</th>
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<tbody>
<tr>
<td>Male (%)</td>
<td>142 (85)</td>
</tr>
<tr>
<td>Age (years ± standard deviation; SD)</td>
<td>58.1 (±13.3)</td>
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<tr>
<td>Family history of SCD (%)</td>
<td>14 (8)</td>
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<tr>
<td>Prospective enrollment (%)</td>
<td>140 (83)</td>
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<tr>
<td>In-hospital SCD (%)</td>
<td>30 (18)</td>
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<td>Estimated time to advanced CPR initiation (minutes ±SD)</td>
<td>6.5 (±6.2)</td>
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<td>- Basic CPR prior to advanced CPR (%)</td>
<td>107 (64)</td>
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<tr>
<td>- No basic CPR prior to advanced CPR (%)</td>
<td>29 (17)</td>
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<td>Duration of advanced CPR until return of spontaneous circulation (RoSC) (minutes ±SD)</td>
<td>9.6 (±11.3)</td>
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<td>Number of defibrillation shocks before RoSC (SD)</td>
<td>2.7 (±2.3)</td>
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<td>Left ventricular ejection fraction (%) on admission (SD)</td>
<td>42 (±15)</td>
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<tr>
<td>Temperature management in acute cardiac care units</td>
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<tr>
<td>TTM duration (hours ±SD)</td>
<td>26 (±7.4)</td>
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<tr>
<td>TTM temperature (°C ±SD)</td>
<td>34.1 (±1.5)</td>
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Causes of VI-related SCD:

- STEMI (%) 80 (47)
- NSTEMI (%) 16 (10)
- Chronic ischemic heart disease (%) 20 (12)
- Idiopathic VF (%) 14 (8)
- Idiopathic dilated cardiomyopathy (%) 11 (7)
- Miscellaneous (%) 11 (7)
- Hypertrophic cardiomyopathy (%) 4 (2)
- Long QT syndrome (%) 3 (2)
- Myocarditis (%) 3 (2)
- Brugada syndrome (%) 2 (1)
- Congenital heart disease (%) 2 (1)
- Right ventricular arrhythmogenic cardiomyopathy (%) 1 (1)
- Valvular heart disease (%) 1 (1)

Diagnostic yield of model vs other tools

![Spectral-based model](image1)

![Spectral-based model](image2)

![Spectral-based model](image3)

![Spectral-based model](image4)