**Worksheet** for Evidence-Based Review of Science for Emergency Cardiac Care

**Worksheet author(s)**
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July 25, 2008,  
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**Clinical question.**
In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of a technique for prediction of the likelihood of success of defibrillation (analysis of VF, etc) (I) compared with standard resuscitation (without such prediction) (C), improve outcomes (eg. successful defibrillation, ROSC, survival) (O).

**Is this question addressing an intervention/therapy, prognosis or diagnosis? INTERVENTION**

**State if this is a proposed new topic or revision of existing worksheet:** NEW TOPIC

**Conflict of interest specific to this question**
Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet?  
Eftestøl has authored papers in related areas of research.

**Search strategy (including electronic databases searched).**

Search strategy MA;  
("cardiac arrest"[Title/Abstract]) AND ("survival"[Title/Abstract]) AND ("prediction"[Title/Abstract])  
("waveform analysis"[Title/Abstract]) AND ("cardiac arrest") AND (ventricular fibrillation)

EmBase: ventricular AND defibrillation AND cardiac AND arrest AND survival AND prediction

Cochrane database for systematic reviews: cardiac arrest

AHA EndNote Master Library: defibrillation AND prediction

Search strategy TE:
Search for defibrillation and outcome and ventricular fibrillation in any field in Endnote online search of PUBMED (113), AHA EndNote 7 Master library,(60).

Search using MESH terms: Heart Arrest, Cardiopulmonary resuscitation, Ventricular fibrillation, Electric countershock (combined with AND): Cochrane databases (reviews and trials) (13), Medline (269), EMBASE (88).

Exclude references prior to 2003 or with no mention of VF waveform analysis in abstract and combine references (44)

Identify key articles and reviews among these according to number of citations and search citing articles in ISI Web of Science.

- **State inclusion and exclusion criteria**
  Inclusion: humans, Animal, all ages, both genders, all journals, peer reviewed
  Exclusion: editorial, letter, practice guidelines, abstract only studies, not peer reviewed, did not directly address the question

- **Number of articles/sources meeting criteria for further review:** 37
  Of these twenty-three were LOE 4 and fifteen were LOE 5
# Summary of evidence

## Evidence Supporting Clinical Question

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**Level of evidence**

A = Return of spontaneous circulation  
B = Survival of event  
C = Survival to hospital discharge  
D = Intact neurological survival  
E = Other endpoint  
*Italicics = Animal studies*
### Evidence Neutral to Clinical question

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A = Return of spontaneous circulation  
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### Evidence Opposing Clinical Question

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A = Return of spontaneous circulation  
B = Survival of event  
C = Survival to hospital discharge  
D = Intact neurological survival  
E = Other endpoint  
*Italics = Animal studies*
VF waveform analysis has been shown retrospectively in both animal models of VF CA and ECG monitoring from VF CA patients to have some prognostic value in predicting successful defibrillation, ROSC success and survival. All of this work is retrospective. Multiple waveform parameters have been examined without consensus on the best parameters. No studies have looked at waveform analysis in a prospective way in real time, thus the use of these parameters to improve outcome is not known. The potential benefit of this methodology if successful, would allow for optimization of the time for defibrillation shocks to maximize defibrillation success and minimize the number of unsuccessful shocks and its attendant disruptions during resuscitation efforts.

Results on outcome predictors when reported in different articles, might be difficult to compare when the data set used are different. There might be several reasons for this:

1) Each waveform analysed is connected to a shock outcome. This outcome is mostly defined in relation to the outcome of the following shock resulting in a temporary or stable ROSC. In some cases waveforms prior to first shock are analysed to predict final outcome as stable ROSC/admission to hospital/survival. Most studies use this definition without further exclusion of waveforms.

2) The data sets from various sites might contain data where the actual probability of success is different. This might give different AUC values for the two systems when methods otherwise are the same. Due to such difficulties in comparing results, studies should also analyse the performance of well established predictors like median frequency (or centroid frequency), waveform amplitude and AMSA that might be considered reference predictors. Thus, high or poorly performing predictors might be explained as being a consequence of the data set if reference predictors show same kind of change in performance compared to performance reported when evaluated on other data sets. Another important aspect is that decision rules should be developed from a design data set and tested on a data set not included in the design.

With these methodologic aspects in mind we consider how the development of outcome predictors has evolved during the last 4-5 years. Several predictors have been developed or reevaluated on human cardiac arrest data sets. Many studies report high performance which would be in the performance range recommended in the outcome prediction worksheet from the C2005 evidence evaluation process. Several of the studies reporting performances in this range are of interest as they are based on analysis of human cardiac arrest data. In the following methodology used in these studies are briefly considered:

1) In Snyder 2007, a commercial shock outcome prediction algorithm implemented in a commercial AED on was tested on historic data not used in development of the algorithm.

2) Similarly several studies (Gundersen 2008, Neurauter 2008, Watson 2005, Watson 2004 ) used cross validation techniques,

Other information may be available from the waveform, e.g. the presence of concordant acute MI (Olasveengen 2009,410), CPR quality (Eftestol 2004,10 and Box 2008,265, Gundersen 2009a, Gundersen 2009). In these studies, changes in parameters computed from the ECG waveform is related to other aspects of therapy than the outcome of an immediate defibrillation. In a decision support system this is crucial, as the parameter derived from the waveform should reflect the patient response to therapeutic intervention (so that good/bad quality therapy should be associated to a positive/negative development in the parameter values). The risk of this intervention is minimal, as the ECG signal which would be analyzed is already readily available. The potential risk to the patient might occur if analysis of the ECG waveform in real time caused delays in delivery of care or unduly refocused rescuers care away from resuscitative efforts. Although promising, more work is needed to determine the best parameters to monitor and develop algorithms to apply this prognostic tool in real time.

SUMMARY POINTS:

- VF waveform analysis has been shown only retrospectively in both animal models of VF CA and ECG monitoring from VF CA patients to have some prognostic value in predicting successful defibrillation, ROSC success and survival.
- Multiple waveform parameters have been examined without consensus on the best parameters.
- No studies have looked at waveform analysis in a prospective way in real time, thus the use of these parameters to improve outcome is not known.
- The potential benefit of this methodology if successful, would allow for optimization of the time for defibrillation shocks to maximize defibrillation success and minimize the number of unsuccessful shocks and its attendant disruptions during resuscitation efforts. The risk of this intervention is minimal, as the ECG signal which would be analyzed is already readily available. The potential risk to the patient might occur if analysis of the ECG waveform in real time caused delays in delivery of care or unduly refocused rescuers care away from resuscitative efforts.
KNOWLEDGE GAPS: Specific research required:

- Optimal timing of defibrillation based on wave from analysis
- Factors responsible for changes in VF waveform, (i.e., time of arrest, quality of CPR, drug administration, co-existent acute myocardial infarction)
- Determination of which VF waveform parameter
- Influence of therapeutic hypothermia and patient temperature on VF waveform

Acknowledgements:

Citation List


LOE 5 - poor-swine model - retrospective analysis of VF signal, supportive, examined VF frequency and amplitude and combination predictive of defibrillation outcome.


LOE 4 fair, ECG cardiac arrest traces in 4 sec segments were retrospectively analyzed using the cardioversion outcome predictor (COP) based on wavelet transform signal processing, to predict successful ROSC from non-ROSC. Also used as a measure of CPR quality.


LOE 4, fair, retrospective analysis of VF signals to determine duration of VF in CA patient ECG VF tracings.


LOE 5, poor, supportive, median frequency to estimate VF downtime in 11 swine


LOE 4, fair, supportive, retrospective determination of scaling exponent in VF tracings from 75 patients predictive of first shock defibrillation and survival to hospital discharge.

LOE 4, fair, supportive, centroid frequency, peak power, spectral flatness and energy, high negative predictive value to avoid ineffective shocks.


LOE 4, fair, supportive, retrospective analysis on patient VF tracings to evaluate effect of CPR on 4 VF waveform parameters and ROSC.


NOTES: Retrospective analysis, testing a previously developed outcome predictor on new data. A previously developed outcome predictor (2-dimensional principal component combination (PCA) of centroid frequency (CF), peak power frequency (PPF), energy (ENRG), spectral flatness (SFM)) was tested on new dataset (589 preshock tracings (82 ROSC) in 156 patients) downloaded from different type of defibrillator. Reevaluation of old data using cross validation yielded AUC=0.79 for the training and AUC=0.80 for the testing on the independent data. Sensitivities and specificities for the test data can be read from the ROC curve as Sns=92%, Spc=43-50%.


LOE 5, poor, supportive, swine model, examined VF wavelet amplitude prior to post shock PEA to predict PEA conversion to ROSC.


NOTES: Retrospective analysis of out of hospital human cardiac arrest data. The primary focus of this study was to investigate if patient specific variations in outcome predictor values could be used to update the outcome prediction calculations learning from previous shocks. The data material consisted of 1062 preshock segments (ROS) from 229 patients. As part of this study various outcome predictors were investigated (amplitude spectrum relationship (AMSA), mean-slope (MS), median-slope (MdS), cardioversion outcome predictor (COP)). An increase AUC=0.02-0.04 was achieved in each predictor using ROC analysis with bootstrapping of the predictor values. The AUC values for predictors which can be used in real–time using updating were=0.87, 0.87, 0.86,0.86 for MdS,MS,COP,AMSA respectively.

**NOTES:** Retrospective analysis of out of hospital human cardiac arrest data. The primary focus of this study was to investigate if there are patient specific variations in outcome predictor values. The data material consisted of 530 preshock segments (54 ROSC) from 86 patients. As part of this study various outcome predictors were investigated (amplitude spectrum relationship (AMSA), mean-slope (MS), median-slope (MdS), cardioversion outcome predictor (COP), mean amplitude (MA), centroid frequency (CF)). Straight forward ROC analysis of the predictor values yielded AUC=0.88,0.88, 0.88,0.86,0.79,0.76 for COP,MdS,MS,AMSA,CF,MA respectively.


**NOTES:** A model is fitted to estimate the expected development of a VF parameter (probability of ROSC). The model was used to compute parameter developments at different levels in another data set.


**NOTES:** A model is fitted to explain how a VF parameter (median slope) is affected by parameters describing the quality of chest compression. The model was used to evaluate the importance of the quality parameters in another data set.


**LOE 5, poor, supportive, swine CA model, retrospective analysis of denoised power spectral density (fibrillation power), mean fibrillation frequency and VF mean amplitude predictive of successful defibrillation.**


**LOE 5, poor, non-supportive, swine model, no association noted between median fibrillation frequency and mean fibrillation amplitude and ROSC after prolonged CA treated with endothelin-1, epinephrine of saline."

**LOE 5, poor, supportive, swine CA model, VF mean, median and dominant frequency, bandwidth and frequency noted to be depressed in acute MI prior to VF compared to VF without acute MI (controls).**


**LOE 5, poor, supportive, retrospective analysis of VF patients before countershock, noting higher level of VF waveform irregularity (chaotic behavior) in successful defibrillation.**


**NOTES:** Retrospective analysis of out of hospital cardiac arrest data. In this study outcome predictors based on signal integral (SignInt), amplitude range (Range), peak frequency (PeakFreq), energy between 2 and 7 Hz (E), periodicity (Per) estimated by the parameter Leakage and slope sign. The outcome predictor was based on a Fisher linear discriminant of these predictors. The dataset consisted of 84 fibrillation cases out of a data base of more than 700 episodes to compose a uniform group. The discriminant functions of ROSC and of non-ROSC yielded Sns=62, Spc=80%.


**LOE 5, poor, supportive, rat CA model, to determine optimal CPR time prior to defibrillation looking at VF amplitude and frequency changes.**


**LOE 5, poor, supportive, swine LAD occlusion, VF model, optimal vs suboptimal CPR on VF amplitude spectrum area values.**


**LOE 5, poor, supportive, swine CA, retrospective analysis of VF scaling exponent - low scaling exponent prior to shock predictive of defibrillation.**

LOE 5, fair, supportive, swine VF CA model, amplitude spectrum area predictive of ROSC.


LOE 5, fair, supportive, swine VF CA model, scaling exponent predictive of post shock defibrillation.


LOE 4, fair, supportive, retrospective analysis of VF waveforms from in and out-of-hospital CA, VF median slope at various frequencies predictive of successful defibrillation.


LOE 4 fair, VF waveforms from 101 CA patients who were categorized into four etiologic categories (1. AMI and no previous treatment for CHD, 2. AMI with previous treatment for CHD, 3. no AMI with previous treatment for CHD, 4. arrhythmia without previous sxs) were retrospectively analyzed using amplitude spectral area (AMSA), centroid frequency (CF), spectral flatness measure (SFM) and median slope (MS) to determine presence of AMI or non AMI. MS and AMSA were significantly depressed in patients with AMI only.


LOE 5, poor, supportive, swine VF CA model, VF amplitude spectrum area predictive of ROSC.


LOE 4, fair, retrospective analysis of VF tracings from CA patients to analyze amplitude spectrum area threshold value predictive of defibrillation.


LOE 5, poor, supportive, retrospective analysis of VF waveform and other factors for prediction of ROSC and neurologically intact survival. Small patient series.

NOTES: Retrospective analysis of data from animal study for derivation of angular velocity (AV) and scaling exponent (SC) based estimation of time in cardiac arrest. In this study 45 ECG of animals were analysed and SC and AV were applied to estimate duration of cardiac arrest. A combination of SC and AV was used to develop a system for discriminating VF with high probability of ROSC from VF with low probability of ROSC. The dataset consisted of ECG from 45 swine with VF developing for 12.5 minutes. Direct analysis for discriminating VF < 5min yielded Sns=90%, Spc=75% for SC+AV combination.


*LOE 5, poor, supportive, swine VF CA model, VF frequency ratio to determine VF duration.*


NOTES: Retrospective analysis of data from animal study and from human out of hospital cardiac arrest data for derivation of logarithm of the absolute correlations in comparison with scaling exponent (SC). In the first part of the study 44 ECG of animals were analysed and SC and AV were applied to estimate duration of cardiac arrest and further to discriminate VF with high probability of ROSC from VF with low probability of ROSC. It was first shown that LAC retains its discriminative power upon down sampling from 1000Hz to 125 Hz while SC does not. The dataset consisted of ECG from 44 swine with VF developing for 12.5 minutes. Direct analysis for discriminating VF < 5min yielded AUC=0.62,0.75 for SC,LAC respectively. For predicting immediate outcome of ROSC in initial shock in 158 patients, direct ROC analysis yielded AUC=0.77,0.57 for SC,LAC respectively with Sns=93%, Spc=30-40% for LAC.


*LOE 4, poor, retrospective analysis of VF tracings from CA patients to analyze “line length” and correlate waveform analysis with neurologic intact survival.*


*LOE 5, poor, supportive, retrospective analysis of VF median frequency, dominant frequency, and amplitude predictive of countershock success, however after eliminating CPR interference, only amplitude was predictive of countershock success.*

LOE 4, poor, supportive, retrospective analysis of VF waveform, specifically an entropy measure provided best specificity and sensitivity in prediction of ROSC.


NOTES: Retrospective analysis of out of hospital human cardiac arrest data. The primary focus of this study was to develop outcome predictors. The data material consisted of 887 preshock segments from 110 patients. Outcome predictors investigated were amplitude spectrum (AMSA), median frequency (MF), spectral energy (SE), wavelet entropy (COP). Cross validated ROC analysis yielded AUC=0.89, 0.69, 0.8, 0.85, Sns=97, 94, 85, 94% Spc=63, 12, 71, 56% for COP, MF, SE, AMSA respectively. In the derivation of these outcome predictors maximum 6 shocks per patient were used.


LOE 4, fair, supportive, retrospective analysis of VF waveform amplitude as a predictor of CA survival.


NOTES: Retrospective analysis of out of hospital human cardiac arrest data. The primary focus of this study was to develop a neural network based outcome predictor. The data material consisted of 198 preshock segments (36 ROSC) from 83 patients. The input to the neural net were delay coordinates of the ECG time series, different lags of 30, 60, 90 and 150 used. Cross validated ROC analysis yielded AUC=0.84, 0.76, 0.72, 0.59, for lags 30, 60, 90, 150 respectively with Sns=83% Spc=67% for lag 30. The sensitivity and specificity results for the other lags are illustrated graphically.


NOTES: Retrospective analysis of out of hospital human cardiac arrest data. The primary focus of this study was to develop outcome predictor using amplitude spectrum area (AMSA). The data material consisted of 108 preshock segments (7 ROSC) from 46 patients. Intervals where perfusing rhythm was maintained for less than 5 seconds were excluded. Direct analysis yielded Sns=91%, Spc=94%.