Resuscitation 120 (2017) 125–131

Contents lists available at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

# Predictive value of amplitude spectrum area of ventricular fibrillation waveform in patients with acute or previous myocardial infarction in out-of-hospital cardiac arrest☆

Michiel Hulleman[a,*], David D. Salcido[b], James J. Menegazzi[b], Patrick C. Souverein[c], Hanno L. Tan[a], Marieke T. Blom[a], Rudolph W. Koster[a]

[a] Department of Cardiology, Heart Center, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands
[b] Department of Emergency Medicine, University of Pittsburgh Medical Center, Pittsburgh, PA, USA
[c] Division Pharmacoepidemiology and Clinical Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, The Netherlands

ARTICLE INFO

*Article history:*
Received 1 May 2017
Received in revised form 30 July 2017
Accepted 20 August 2017

*Keywords:*
Cardiopulmonary resuscitation
Heart arrest
Sudden cardiac death
Arrhythmia
ST-segment elevation myocardial infarction
Quantitative waveform measures
Ventricular fibrillation

ABSTRACT

*Background:* Amplitude spectrum area (AMSA) of ventricular fibrillation (VF) has been associated with survival from out-of-hospital cardiac arrest (OHCA). Ischemic heart disease has been shown to change AMSA. We studied whether the association between AMSA and survival changes with acute ST-elevation myocardial infarction (STEMI) as cause of the OHCA and/or previous MI.
*Methods:* Multivariate logistic regression with log-transformed AMSA of first artifact-free VF segment was used to assess the association between AMSA and survival, according to presence of STEMI or previous MI, adjusting for resuscitation characteristics, medication use and comorbidities.
*Results:* Of 716 VF-patients included from an OHCA-registry in the Netherlands, 328 (46%) had STEMI as cause of OHCA. Previous MI was present in 186 (26%) patients. Survival was 66%; neither previous MI (P = 0.11) nor STEMI (P = 0.78) altered survival. AMSA was a predictor of survival (ORadj: 1.52, 95%-CI: 1.28–1.82). STEMI was associated with lower AMSA (8.4 mV-Hz [3.7–16.5] vs. 12.3 mV-Hz [5.6–23.0]; P < 0.001), but previous MI was not (9.5 mV-Hz [3.9–18.0] vs 10.6 mV-Hz [4.6–19.3]; P = 0.27). When predicting survival, there was no interaction between previous MI and AMSA (P = 0.14). STEMI and AMSA had a significant interaction (P = 0.002), whereby AMSA was no longer a predictor of survival (ORadj: 1.03, 95%-CI: 0.77–1.37) in STEMI-patients. In patients without STEMI, higher AMSA was associated with higher survival rates (ORadj: 1.80, 95%-CI: 1.39–2.35).
*Conclusions:* The prognostic value of AMSA is altered by the presence of STEMI: while AMSA has strong predictive value in patients without STEMI, AMSA is not a predictor of survival in STEMI-patients.


## Introduction

Early defibrillation for ventricular fibrillation (VF) is the most important predictor of survival from out-of-hospital cardiac arrest (OHCA) [1]. VF morphology may have additional value to predict chances of survival, and can be quantified by continuous VF waveform measures, based on amplitude, frequency, power spectrum, and coarseness of the signal [2]. In particular, VF amplitude and frequency decline with increasing time delay from collapse to initial rhythm assessment (call-to-ECG delay); this decline correlates with decreases of high energy phosphates in myocardial cells and coronary perfusion pressure [3,4], and can be slowed or reversed by cardiopulmonary resuscitation (CPR) [5,6]. Accordingly, amplitude spectrum area (AMSA) is one of the most often used quantitative VF waveform measures.

In general, higher VF waveform measures (e.g., higher AMSA) have been associated with higher survival rates in multiple observational studies [7–10]. This is generally ascribed to their strong correlation with favorable resuscitation characteristics (e.g., public location, bystander witnessed collapse, bystander CPR, short call-to-ECG delay) [9]. However, patient characteristics may also impact on AMSA and/or survival chances. Ischemic heart disease (both acute and previous myocardial infarction [MI]) has been shown to affect VF waveform measures [11–16]. We therefore studied whether AMSA may predict survival from OHCA in relation to either

☆ A Spanish translated version of the abstract of this article appears as Appendix in the final online version at http://dx.doi.org/10.1016/j.resuscitation.2017.08.219.

* Corresponding author at: Department of Cardiology, room G4-248, Academic Medical Center, University of Amsterdam, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands.
*E-mail address:* m.hulleman@amc.nl (M. Hulleman).

http://dx.doi.org/10.1016/j.resuscitation.2017.08.219

acute STEMI as cause of their OHCA or with previous MI in their history, or both.

## Methods

### *Study design, setting and patient selection*

The present study used data from the ARREST (AmsteRdam REsuscitation STudies) database, an ongoing prospective registry of all resuscitation attempts in the North-Holland province of The Netherlands [18]. This province has a population of 2.4 million people and covers 2671 $km^2$, with both urban and rural communities, including Amsterdam. We included all patients with OHCA from cardiac causes between July 2005 and December 2011 with electrocardiogram (ECG) VF recordings from LIFEPAK (Physio-Control, Redmond WA, USA) automated external defibrillators (AED) or manual monitor-defibrillators (these defibrillators constitute >90% of all used defibrillators in the study region). We excluded patients with OHCA from clear non-cardiac causes (i.e., drowning, trauma, neurologic causes) or whose medical history or medication use could not be retrieved. The study cohort included the patients who were admitted to hospital, to be able to establish a reliable ST-elevated MI (STEMI) diagnosis using hospital diagnostics.

All data were collected according to the Utstein recommendations [17]. Written informed consent was obtained from all participants who survived the OHCA. The Medical Ethics Review Board of the Academic Medical Center, Amsterdam, approved the study, including the use of data from patients who did not survive the OHCA.

### *Data collection*

Data collection of the ARREST registry has been described in detail elsewhere [18]. In short, for all suspected OHCA calls, dispatch forms with time stamps of start of EMS call and EMS dispatch are collected. After each resuscitation attempt, paramedics routinely send the digital continuous ECG recording from their manual defibrillators to the study center. If an AED was also attached, study personnel collects the ECG recording from the AED. The clock times of AED and manual defibrillator recordings are synchronized with a network clock. Initial rhythm from ECG recordings from ambulance manual defibrillator or AED are assessed by study personnel shortly after the OHCA. The impedance channel from the AED or manual defibrillator is used to establish when chest compressions were being given.

Resuscitation characteristics are collected from the dispatch center, first responders, paramedics and hospitals. Complete medication use in the year preceding the OHCA is obtained from the patient's pharmacy. Medical history of the patients is obtained from the general practitioner (GP) by a study questionnaire. In The Netherlands, virtually every citizen has a GP, and the GP acts as gatekeeper for specialist medical care. Accordingly, the GP receives all medical correspondence. When information from a patient's GP could not be retrieved, information on medical history is retrieved from hospital records if available.

Survival to emergency department (ED), survival to hospital admission and survival to hospital discharge is retrieved from the hospital records. Survival to admission is known from the paramedics run sheet.

### *Definitions*

The primary outcome was survival to hospital discharge, with AMSA as the main predictor variable. AMSA represents a summation of the frequencies in the VF signal weighted by their corresponding amplitudes [19]. To calculate AMSA, ECG signals were exported with a sample rate of 125 Hz using Research Exporter (Physio-Control, version 1.2). All digitized signals were exported to MATLAB (R2014B, the Mathwork Inc) for further processing. The first movement and chest compression artifact-free VF segment was manually selected for analysis. Segments of 2–5 s artifact-free VF were band-pass filtered between 4 and 48 Hz. Using a fast Fourier transformation, ECG signals were transformed into the frequency domain. To control for any increase in AMSA from first analyzable segment to first defibrillation, the AMSA immediately before the first shock was also calculated. The waveform analysis was performed by one reader (MH) who was blinded to any patient information at the time of analysis.

We assessed whether STEMI was the cause of the OHCA, and whether previous MI was present in the patient's medical history. Diagnosis of STEMI was based on available 12-lead ECGs (ST elevation of $\geq$0.1 mV elevation in at least two adjacent limb leads or >0.2 mV in two adjacent precordial leads) and evidence of transmural ischemia (using troponins, CK-MB and autopsy reports). As the diagnosis STEMI can only reliably be made in-hospital, we only included patients who were admitted to the hospital in this study. Patients with non-STEMI (elevated cardiac enzymes without ST-elevation) were not included in the group with STEMI patients. Patients were considered to have a previous MI if confirmed by the patient's GP on a questionnaire, or from hospital records. From hospital case files we also assessed whether a coronary angiogram (CAG), revascularization, internal cardioverter defibrillator (ICD) implantation, intensive care unit (ICU) admission or therapeutic hypothermia was performed.

As possible confounders, we considered the effect of common cardiovascular medications that could be prescribed following a previous MI. Medication use was classified according to the Anatomical Chemical Therapeutic (ATC) code of the World Health Organization (WHO) [20]. Patients were considered users during OHCA if the prescription window covered the date of the OHCA. We included beta-blockers (ATC CO7), ACE-inhibitors (ATC C09A), anti-platelet therapy (ATC B01AC), lipid modifying medication (ATC C10AA) and loop-diuretics (ATC C03C). We also included heart failure (as a possible consequence of a previous MI) and hypertension (related to the prescribed medication) as potential confounders. These diagnoses were considered present if this was indicated on the questionnaire filled out by the GP, or on hospital case files.

The timestamp of EMS call and time of initial rhythm recording from manual defibrillator or AED was used to calculate the time delay between EMS call and initial rhythm recording and was defined as call-to-ECG delay. Other resuscitation characteristics that were included in the analyses were number of defibrillations, presence of EMS- or bystander witness and performance of bystander CPR.

### *Data analysis*

Proportions were shown as n (%), using Chi-Square test to test for significance. AMSA and time intervals had a non-normal distribution and were expressed as median (interquartile range (IQR)), with differences tested using Mann-Whitney *U* tests. Results from these univariate tests were confirmed using multivariate linear regression analysis on log transformed AMSA including all demographics, resuscitation characteristics, medication use and comorbidities. The difference between AMSA of first analyzable segment and AMSA before first shock was calculated using a paired samples *t*-test.

We compared median AMSA in STEMI patients and patients without STEMI in relation to call-to-ECG delay using Mann-Whitney *U* tests. To analyze whether the decrease in AMSA over time was different for STEMI and non-STEMI patients, a linear regression analysis was performed with log transformed AMSA,