Resuscitation 80 (2009) 946–950

Contents lists available at ScienceDirect

Resuscitation

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

Experimental paper

# Association of intramyocardial high energy phosphate concentrations with quantitative measures of the ventricular fibrillation electrocardiogram waveform☆

David D. Salcido[a,*], James J. Menegazzi[a], Brian P. Suffoletto[a], Eric S. Logue[a], Lawrence D. Sherman[b]

[a] Department of Emergency Medicine, University of Pittsburgh, Pittsburgh, PA, United States
[b] Emergency Department, St. Francis Hospital, Federal Way, WA, United States

ARTICLE INFO

*Article history:*
Received 27 January 2009
Received in revised form 1 April 2009
Accepted 4 May 2009

*Keywords:*
Ventricles
Fibrillation
Metabolism
Electrocardiography
Death
Sudden

ABSTRACT

*Background:* Quantitative measures of the ventricular fibrillation (VF) electrocardiogram (ECG) have been correlated with the success of rescue shocks, making them ideal measures for guiding resuscitative interventions. Correlation of intramyocardial energy stores with the change in quantitative VF ECG measures would provide mechanistic insight into their utility. We sought to investigate the relationship between intramyocardial energy stores and four quantitative ECG measures.
*Methods:* Eighteen mixed-breed, domestic swine were sedated, anaesthetized and paralyzed. Swine were block randomized into three groups receiving 5, 10, or 15 min of untreated VF. Thoracotomy was performed and the heart was delivered. VF was induced by a 100 mA transthoracic shock while ECG was recorded. Biopsies of myocardial tissue were taken from the left and right ventricles after the prescribed duration of VF. Adenosine triphosphate (ATP) and adenosine diphosphate (ADP) concentrations in the tissue samples were measured. ECG data immediately prior to each biopsy were analyzed by each of four quantitative ECG methods: Scaling Exponent (ScE), Median Slope (MS), Amplitude Spectrum Area (AMSA), and logarithm of the Absolute Correlation (LAC). ATP and ADP concentrations of VF duration groups were compared. ATP and ADP concentrations were regressed against each quantitative ECG measure.
*Results:* ATP concentrations differed between VF duration groups, but ADP concentrations differed only between 5 and 10 min groups. A significant association existed between ATP and three quantitative measures – ScE, MS, and AMSA – but no significant relationship was found for ADP.
*Conclusion:* Intramyocardial ATP levels correlate with quantitative measures of the ECG during ventricular fibrillation.



## 1. Introduction

Analysis of the electrocardiogram (ECG) during ventricular fibrillation (VF) has led to the development of quantitative measures useful for interpreting the VF waveform for clinical purposes. These include measures based on amplitude, frequency, and geometry.[1–4] Examples include Mean/Median Frequency (MF), Median Slope (MS), Amplitude Mean Spectrum Area (AMSA), and logarithm of the Absolute Correlation (LAC).[3] The VF Scaling Exponent (ScE) is a non-linear geometric measure of the ECG waveform that estimates the fractal dimension of the ECG waveform during VF. The ScE has been demonstrated to be directly proportional to duration of untreated cardiac arrest.[2] The progression of ScE from low (1.1) to high (1.8) corresponds to a decrease in cardiac susceptibility to defibrillating shocks, as demonstrated by reduction in probability of ROSC with increasing ScE in animal and human studies.[5–7]

The time dependent relationship between the Scaling Exponent and the success of rescue shocks may be rooted in the relationship between duration of untreated VF and intramyocardial energy stores. High energy phosphate stores in the myocardium during untreated VF have been demonstrated to rapidly and continuously decrease over time.[8] Elucidation of the relationship between depletion of available energy stores and progressive increase in Scaling Exponent could provide mechanistic insight into the predictive utility of the Scaling Exponent for defibrillation suc-

☆ A Spanish translated version of the summary of this article appears as Appendix in the final online version at doi:10.1016/j.resuscitation.2009.05.002.

* Corresponding author at: Department of Emergency Medicine, Iroquois Building, Suite 400A, 3600 Forbes Ave, Pittsburgh, PA 15216, United States.
Tel.: +1 412 647 3078.
*E-mail address:* salcidodd@upmc.edu (D.D. Salcido).

0300-9572/$ – see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.resuscitation.2009.05.002

cess, as well as provide an electrophysiological tool for gauging intra-arrest pharmacological therapies intended to facilitate resuscitation.

We sought to examine the extent to which intramyocardial high energy phosphate stores correlate with the quantitative measures of the ECG during untreated VF. Employing a swine model of prolonged ventricular fibrillation, we investigated the relationship between a range of Scaling Exponent measures and adenosine triphosphate (ATP) and adenosine diphosphate (ADP) levels in myocardial tissue. We extended this analysis to three other quantitative measures for comparison.

## 2. Methods

### 2.1. Animal preparation

This study was approved by the University of Pittsburgh Institutional Animal Care and Use Committee.

Eighteen mixed-breed, domestic swine were sedated with ketamine (10.0 mg/kg) and xylazine (4.0 mg/kg), intubated with a 5-0 cuffed endotracheal tube, and anaesthetized with alpha chloralose (50 mg/kg bolus followed by 10 mg/kg/h). The animals were ventilated mechanically with an Ohmeda 7000 ventilator (BOC Health Care, Madison, WI) at a rate of 12 breaths per minute with an inspiration:expiration ratio of 50%. Animals were paralyzed with pancuronium (4 mg bolus, 2 mg additional as needed), and a cut-down was performed on the right-side groin to expose the femoral artery and vein. From this entrance site, micro-manometer tipped pressure catheters (Mikro-Tip Catheter Transducers SPR-471A and SPC-370-S, Millar Instruments, Houston, Texas) were placed in the aorta and right atrium, respectively, for monitoring of central blood pressures. The electrocardiogram was monitored continuously with Lead II ECG and recorded along with central pressure data with a high speed digital data collection system (Powerlab, AD Instruments NSW, Australia). Baseline blood gas measurements were obtained with an I-STAT Portable Clinical Analyzer (Heska Corporation, Waukesha, WI).

Each swine was block randomized into 1 of 3 groups to undergo 5, 10 or 15 min of untreated VF. Experimenters were not blinded to group identity. Prior to cardiac arrest, the chest was opened and the pericardium was removed, exposing the heart. Ventricular fibrillation was induced by a 3-s, 60 Hz, 100 mA transthoracic shock. Cardiac arrest was verified by visual inspection of the aortic pressure tracing, and ventricular fibrillation was verified visually by inspection of the ECG waveform. A digital timer was started at the onset of arrest. After the prescribed duration of ventricular fibrillation, punch biopsies were taken from the left ventricle (LV) and right ventricle (RV) of the fibrillating heart. Care was taken to minimize tissue extraction time with an average time on the order of 50 s.

Each tissue sample was immediately transferred to a dry ice/isopentane slurry (−79 °C) for flash freezing. Frozen samples were then transferred to individual liquid nitrogen-cooled stainless steel mortars, which were segregated by tissue region, and pulverized with a chilled pestle. Small quantities of each myocardial tissue sample were then suspended in 1 mL of chilled 1% trichloroacetic acid extraction buffer contained in pre-weighed microcentrifuge tubes. The tubes were re-weighed to measure the mass of each suspended tissue specimen. Suspended samples were then transferred on ice to a microcentrifuge and spun at 4500 rcf for 10 min to pellet-out solid tissue fragments. One hundred microliters of supernatant from each extracted specimen were subsequently diluted 1/10 in TAE buffer pH 7.75. Diluted samples and remaining extracted material were frozen at −70 °C until analysis could be performed.

**Table 1**
Baseline physiological values by VF duration group.

| | Wgt (kg) | HR (BPM) | Temp (°C) | SBP (mmHg) | DBP (mmHg) | Anest (min) | pH | $pCO_2$ (mmHg) | $pO_2$ (mmHg) | $O_2$ Sat (%) | Glu (mg/dL) | Bicarb (mM) | Na+ (mM) | K+ (mM) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 5 min | | | | | | | | | | | | | | |
| *N* | 6 | 6 | 6 | 6 | 6 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 26.6 | 113.1 | 38.0 | 123 | 84 | 29.8 | 7.44 | 38.8 | 76.8 | 95.7 | 109.8 | 27.4 | 142.2 | 3.8 |
| Std Dev | 2.4 | 24.1 | 0.6 | 10 | 8 | 6.5 | 0.03 | 3.2 | 7.0 | 1.5 | 12.7 | 3.0 | 1.7 | 0.2 |
| 10 min | | | | | | | | | | | | | | |
| *N* | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 5 | 6 | 6 | 6 |
| Mean | 26.0 | 114.0 | 38.0 | 133 | 93 | 28.2 | 7.47 | 36.6 | 81.2 | 96.7 | 128.8 | 27 | 142.8 | 3.5 |
| Std Dev | 1.1 | 11.9 | 0.7 | 18 | 14 | 2.1 | 0.03 | 1.8 | 9.2 | 1.0 | 22.7 | 2.6 | 1.5 | 0.2 |
| 15 min | | | | | | | | | | | | | | |
| *N* | 6 | 5 | 6 | 5 | 4 | 6 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean | 25.4 | 118.8 | 38.5 | 132 | 85 | 28.8 | 7.50 | 36.0 | 76.8 | 96.4 | 109.4 | 28.2 | 142.2 | 3.7 |
| Std Dev | 0.8 | 9.8 | 0.7 | 8 | 2 | 2.6 | 0.03 | 2.7 | 3.1 | 0.5 | 23.9 | 1.6 | 1.3 | 0.2 |

*Abbreviations*: Wgt (weight), HR (heart rate), SBP (systolic blood pressure), DBP (diastolic blood pressure), Anest (anaesthesia time), Glu (glucose), Bicarb (bicarbonate ion).