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ScienceDirect
Journal of Electrocardiology 42 (2009) 527–533
JOURNAL OF Electrocardiology
www.jecgonline.com

# Changes in the frequency spectrum, the P-P interval, and the bispectral index during ventricular fibrillation are physiologic indicators of ventricular fibrillation duration

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Received 22 April 2009

**Abstract** The 3-phase time-sensitive model by Weisfeldt and Becker in 2002 has resulted in a redirection of efforts toward developing treatment algorithms specific to each phase of cardiac arrest. In this study, a number of physiologic indicators of ventricular fibrillation (VF) duration were investigated. The bispectral index was recorded at 15-second intervals over 12 minutes and recordings of the atrial electrocardiogram and lead II electrocardiogram were acquired simultaneously using Notocord data acquisition software during sinus rhythm, ventricular tachycardia, and VF, and analyzed using a total of 30 porcine models. A number of frequency markers (fast Fourier transform and density and amplitude of peaks [DA]) were derived. There was a direct relationship between VF duration and bispectral index with a Pearson correlation coefficient (mean) of $r = -0.91$. The P-P interval recorded in the atria during VF, demonstrated similar findings ($r = 0.97$) when measured against VF duration. It was interesting to note that P waves were still apparent during VF despite the on-going chaotic activity in the ventricles. The DA was calculated for each episode of prolonged VF and an exponential relationship with VF duration was observed. The dominant frequency during VF, DA, the P-P interval, and the BIS index are all potential physiologic indicators of VF duration.


*Keywords:* Ventricular fibrillation; Atrial ECG; P wave; P-P interval; Bispectral index

## Introduction

In spite of the development and periodic review of guidelines with the aim of optimizing resuscitation procedures, survival from cardiac arrest in the industrialized world remains dismal.[1] In the absence of early defibrillation, survival beyond the electrical phase (within 4 minutes) of cardiac arrest is predominantly dependent on coronary and cerebral perfusion pressures, both of which are generated by chest compressions.[2,3]

Early defibrillation has a prevailing impact on the outcomes of out-of-hospital sudden cardiac arrest of less than 4 minutes in duration. Defibrillation administered by lay providers has resulted in an increase in the rate of initial resuscitation and survival to hospital discharge after sudden cardiac arrest.[4] The benefit of cardiopulmonary resuscitation (CPR) before defibrillation seems only to be apparent in cardiac arrest cases of longer duration.[5] It may be therefore possible to use waveform analysis to determine the duration of a cardiac arrest in real time.

The 3-phase time-sensitive model by Weisfeldt and Becker in 2002 has resulted in a redirection of efforts toward the development of treatment protocols specific to each phase of cardiac arrest.[6,7] The model suggests that defibrillation should be administered within the first 4 minutes of a cardiac arrest, known as the electrical phase.[6,7] Cardiopulmonary resuscitation is the recommended treatment of arrests of duration between 4 and 10

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doi:10.1016/j.jelectrocard.2009.06.010

minutes, known as the circulatory phase. At an appropriate level, after the provision of adequate circulatory support, defibrillation should be advised. Finally, the metabolic phase refers to arrests of longer than 10 minutes.

Previously investigated methods such as fast Fourier transform (FFT) analysis during ventricular fibrillation (VF) were explored (to extract the dominant frequency). In addition, previously unexplored parameters including the patients' electroencephalogram (EEG) (using the bispectral [BIS] index) and observations of the electrical activity in the atria (P wave) during VF were investigated. The aforementioned techniques have not been previously reported by other research groups. Parameters that have been previously investigated as indicators of VF duration are described in more detail in the Discussion section.

The BIS index is commonly used to monitor the depth of anesthesia (level of consciousness) in a surgical patient. It can be used to indicate the level of cerebral activity noninvasively and was therefore an ideal measurement apparatus for this study, but it has also recently been investigated as a tool to monitor outcomes after CPR.[8] The BIS index scale ranges from 0 to 100 indicating the patient is fully aware and conscious. The BIS monitor provides a single dimensionless number, with a BIS value of between 40 and 60 indicating a level suitable for general anesthesia.[9] Although a number of other parameters have been explored as potential indicators of VF duration,[10-14] both the P-P interval and the density and amplitude of peaks (DA) have not been previously investigated. In addition, this is the first study of its kind to report on the activity in the atria during an episode of prolonged VF.

## Materials and methods

### *Preparation*

This research was carried out in accordance with the United Kingdom Animals (Scientific Procedures) Act of 1986. The animals were sedated with subcutaneous azaperone (1-2 mg/kg), anesthetized with pentobarbitone (30 mg/kg IV; Sagatal, Rhône Mérieux Ltd, Harlow, UK), intubated with a 9F endotracheal tube, and ventilated with room air (Model 16/24, Ideal respirator, CF Palmer Ltd, London, UK). Pentobarbitone was subsequently supplemented as needed to maintain an adequate level of anesthesia. One venous sheath was inserted in the left external jugular vein followed by one arterial sheath in left common carotid artery. A temporary pacing line is fed through the left venous sheath to the right ventricle. Finally, an arterial line was inserted to record the blood pressure. The surface ECG (lead II) and arterial blood pressure tracings were displayed and saved on Notocord-hem (version 0.08, 2005). Core body temperature, oxygen saturation, and tidal carbon dioxide levels were monitored throughout the experiment. Temperature was maintained within normal limits by using a homeothermic water-heated blanket.

### *Measurements*

One standard defibrillator (HeartSine Technologies, Ltd, Belfast, Northern Ireland) was used to monitor the animal's ECG (lead II) externally. In addition to the standard external measurements, a third venous line was inserted. This additional line enabled the insertion of a standard monitoring electrode array into the right atrium to allow observation of the electrical activity within the atrium during sinus rhythm and VF. Real-time recordings were taken from the right atrium using a multielectrode array (Elecath 6-7F). Simultaneous recordings of the surface ECG were made via 2 standard defibrillation electrodes. The outputs from both the preamplifier (internal recordings of the atrial ECG amplified by a gain factor of 10) and the outputs from the ECG monitor/defibrillator were displayed continuous using Notocord data acquisition system. Therefore, there were 2 separate channels of information displayed and no signal extraction was required.

### *Protocol*

Defibrillation electrodes (ST&D Ltd, Belfast, Northern Ireland) were placed over the right upper chest/sternum and over left apex. All Impedence Cardiography, ECG, blood pressure, and P wave (electrical activity in the atria) recordings were made electronically using the Notocord acquisition system for subsequent analysis. The pulse oximetry measurements were taken from the upper lip of the porcine model. Initial recordings of sinus rhythm were then taken. The BIS monitor (Aspect Medical Inc, Norwood, MA) was connected and the accompanying adult electrode array was adhered to the animal model's forehead after lightly abrading the area of application. The BIS monitor was switched into self-test mode to ensure good electrode-skin contact by passing or failing each of the 4 individual gel electrode sites found in each electrode.

Ventricular fibrillation was induced using a Grass stimulator (Grass Technologies, West Warwick, RI, USA), and the EEG, atrial ECG, and ECG (lead II) were recorded and displayed using Notocord. The model was left in VF for approximately 12 to 15 minutes or less depending on the model's physiologic response to induced VF. The EEG was recorded at 15-second intervals over the duration of VF (12-15 minutes).

### *Analysis*

During observational analysis, it was noted that atrial depolarization was still occurring during VF. The P waves present during VF also coincided with peak amplitudes of each VF envelope as shown in Fig. 1B. It was also observed that over time, the P-P interval increased during VF. The P-P interval was measured for each of the 10 cases during prolonged VF; this was completed manually using the measurement tool available in the Notocord analysis package. The distances were then plotted against the noted times using Microsoft Excel.

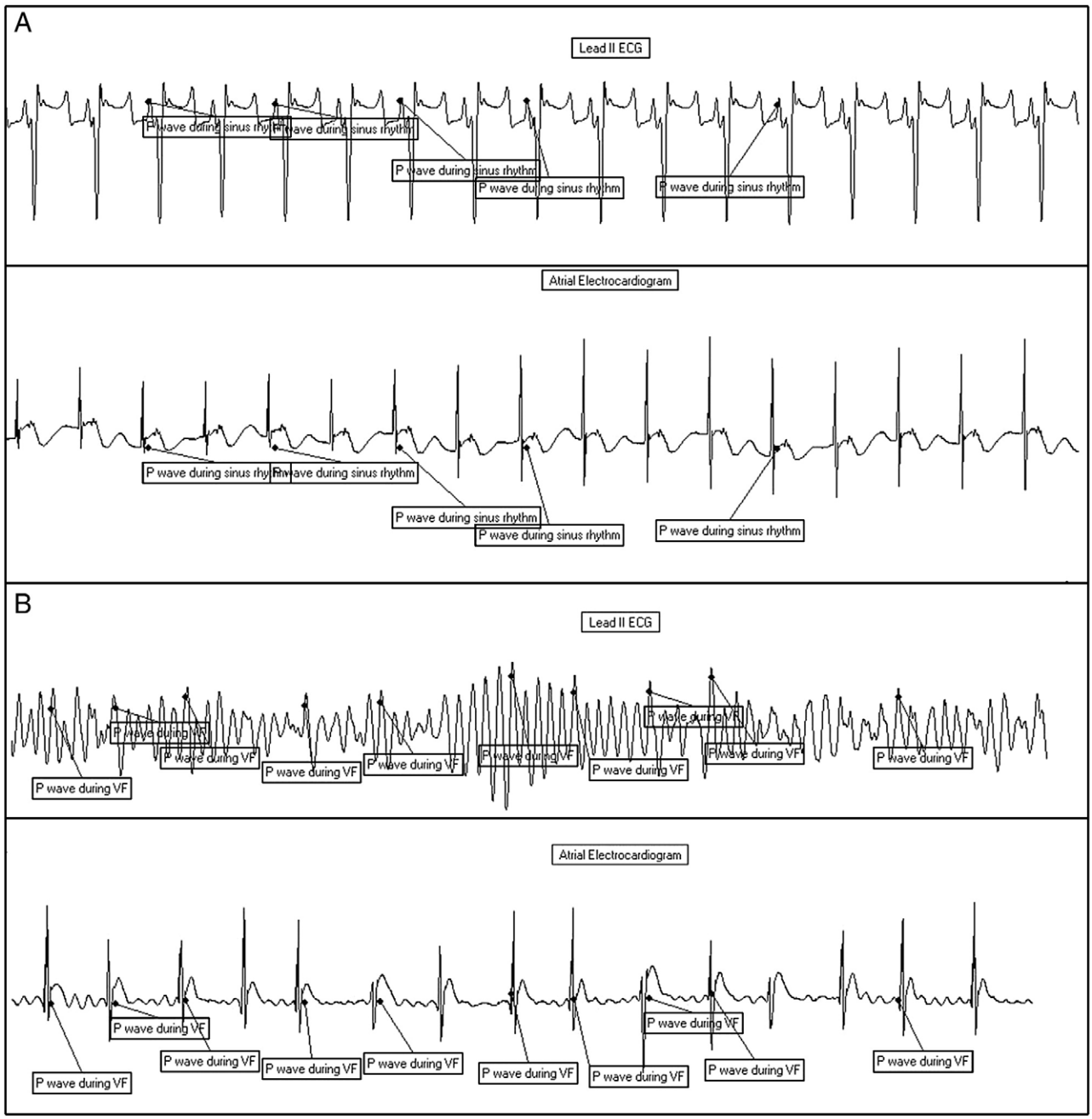


Fig. 1. Simultaneous recordings of the atrial activity during (A) sinus rhythm and (B) VF. P waves are labeled to illustrate how the P wave and the peak amplitude of each VF envelope coincide.

*Calculations*

A sequence of ECG samples $x_0, x_1, \ldots, x_{N-1}$ in a window of $N$ samples is processed to obtain the DA:

$$\mathrm{DA} = \frac{1}{N}\sum_{i=0}^{N-1} w_i, \quad \textit{where}$$

$$w_i = \begin{cases} |x_i| \text{ if } |x_i| \text{ is a peak} \\ 0 \text{ otherwise} \end{cases}$$

A "peak" here is defined as a value outside an amplitude varying envelope containing the ECG signal. To calculate the envelope, the ECG rectified signal is used where the absolute value of the samples is calculated. The principle in deriving the envelope was to construct a ray aiming at the baseline at a particular rate, but the ray could be reset by a sample "obstructing" its path to the baseline.

*Algorithm development*

A retrospective analysis of a number of cases of prolonged VF enabled the selection of an appropriate cutoff point between the end of the electrical phase and the start of the circulatory/metabolic phase of VF. For the algorithm shown in Fig. 2A, the envelope or minimum threshold of the VF signal over a window of N samples is self-adjusting for each individual case. Therefore, there is no fixed amplitude criterion, but DA for 12 seconds (2048 samples) is calculated and the result is updated for every sample (moving average).

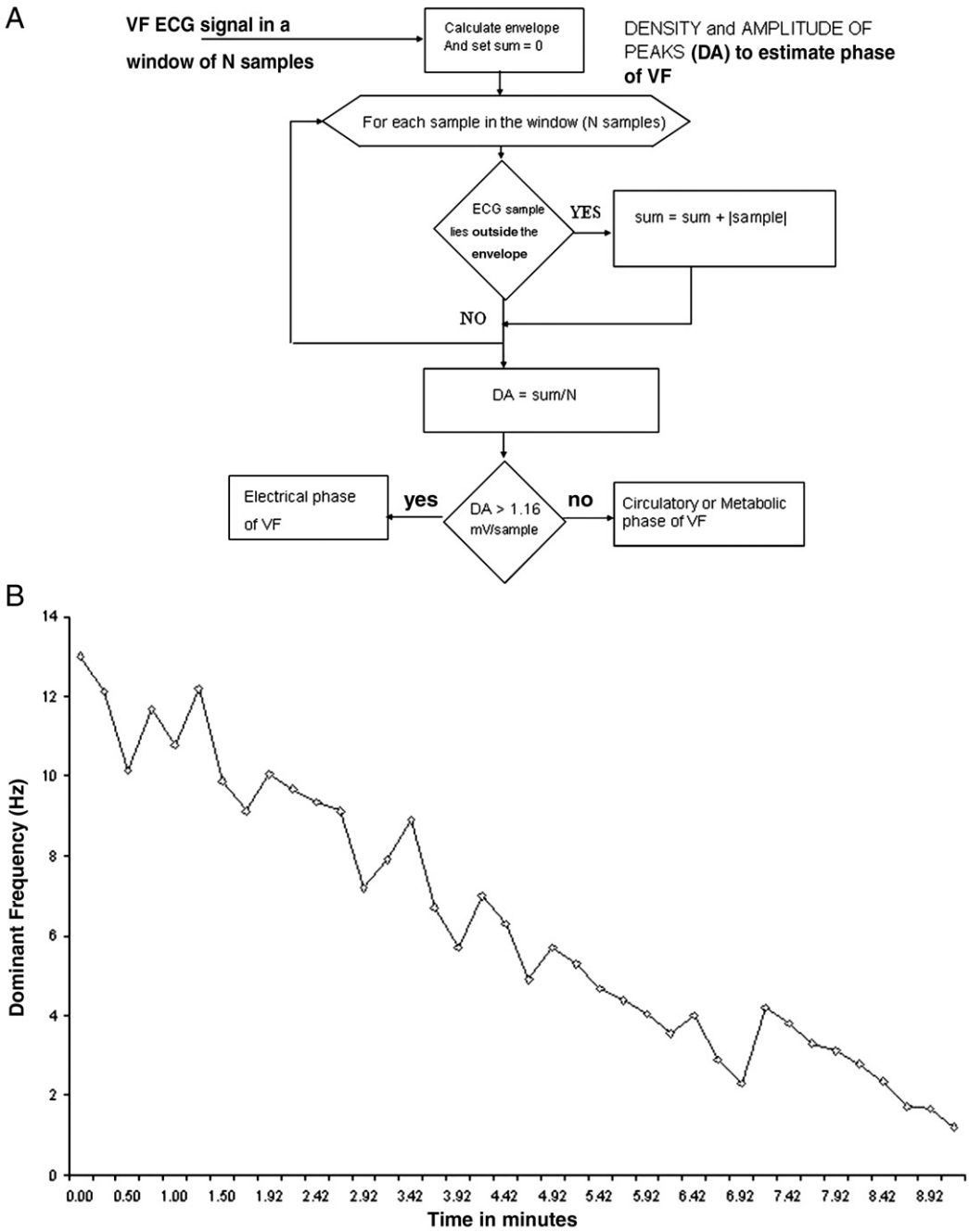


Fig. 2. A, A flow diagram showing how the algorithm will determine whether a patient is in the electrical phase or not. The algorithm uses ECG analysis to determine the DA. B, Graph showing the changes in dominant (peak) frequency (using FFT) over time during an episode of prolonged VF.

If DA falls less than 1.16 mV/ sample, then the VF signal is said to be in either the circulatory or metabolic phase (CPR would be advised as the most appropriate treatment in this patient). If DA is higher than 1.16 mV/ sample, then the VF signal is more likely to be in the electrical phase of cardiac arrest and the advised treatment would be defibrillation.

## Results

Qualitative and quantitative observations of the P wave were made during VF in 10 porcine models. In addition, the FFT and DA were obtained retrospectively using a custom-made program in C language and Excel, again using a further 10 models. Simultaneous recordings of the BIS index (EEG) were made during VF (10 models). During these experiments, a total of 30 porcine models (mean ± SD weight,

Table 1
Mean ± SD of recordings before the onset of cardiac arrest

| Initial recordings | |
|---|---|
| Weight (kg) | 51.3 ± 1.2 |
| Rectal temperature | 36.4 ± 0.4°C |
| $Spo_2$ | 97 ± 1.2 |
| $ETco_2$ (mm Hg) | 34 ± 2.1 |
| Arterial blood pressure (mm Hg) | 118/63 |

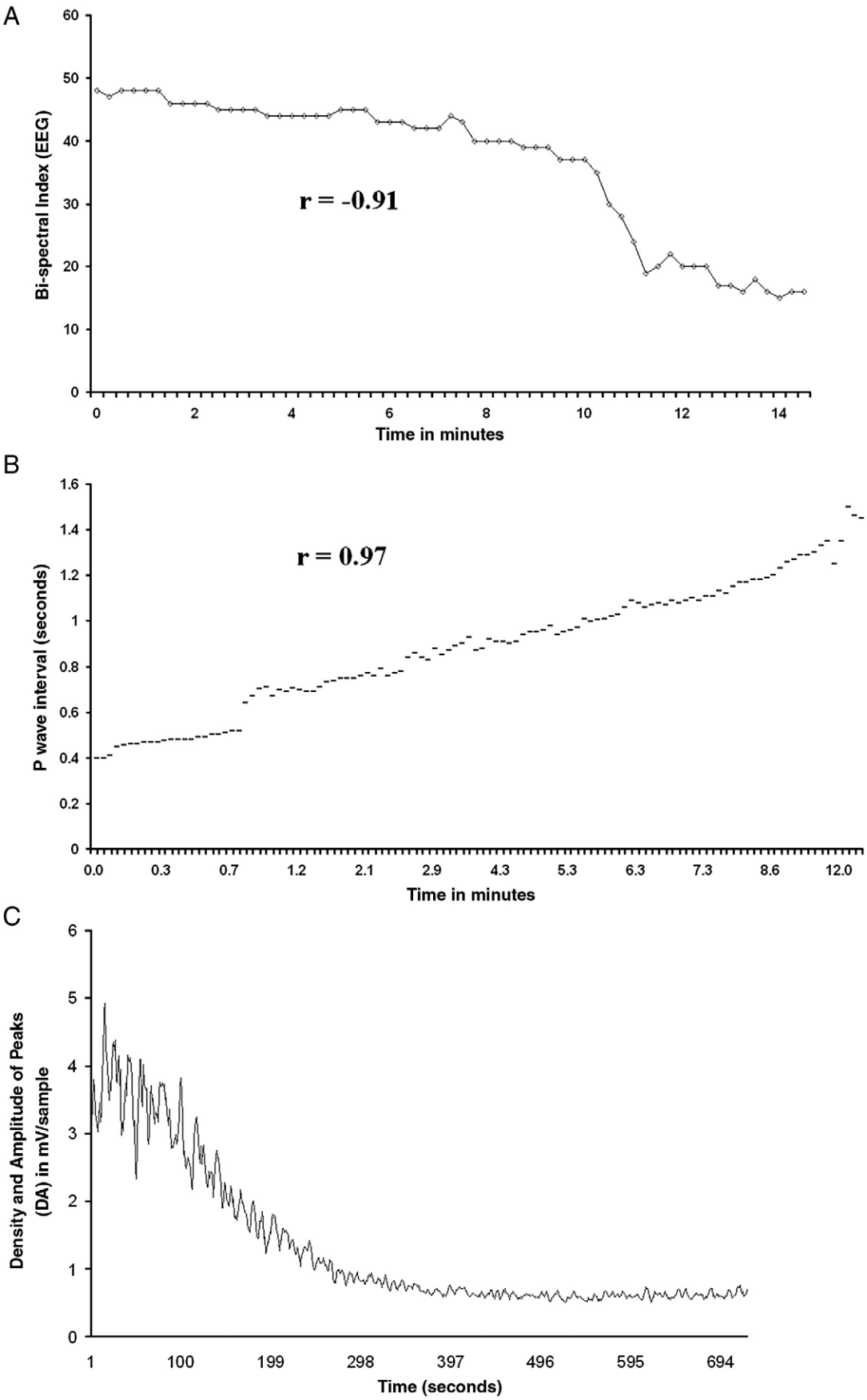


Fig. 3. A, Graph showing the relationship between the BIS index (EEG) and time during VF in minutes. B, Graph showing the relationship between the P-P interval and time during VF in minutes and the relevant phases of cardiac arrest to which they belong. C, Graph showing changes in the DA over time during a 12-minute episode of VF.

51.3 ± 1.2 kg) were used; of these, 10 were used during the P-wave recordings. The average rectal temperature and $Spo_2$ of the 30 models used was 36.4°C ± 0.4°C and 97% ± 1.2% with an $ETco_2$ of 34 ± 2.1 mm Hg. The initial readings are summarized in Table 1.

Quantitative analysis of the VF waveform using firstly FFT analysis (FFT of VF vs time during VF in seconds) resulted in a Pearson correlation coefficient of $r = -0.94$ (mean over 10 experiments) as shown in Fig. 2B. FFT analysis enabled the extraction of the dominant frequency over 4096 samples. Fast Fourier transforms are less economic when applied real-time and, therefore, a different technique was applied, which used less processor power. At the outset of VF, the DA is 4.65 mV/sample. After only 6 to 7 minutes of VF, the DA had decreased significantly to 1.16 mV/ sample. At the initial stages of VF, the porcine model had a BIS index of approximately 48 to 57. After 10 minutes of VF, the BIS index decreased to approximately 20 to 30. After 12 to 15 minutes of VF, the BIS index plummeted to between 13 and 15 (Fig. 3).

## Discussion

The importance of delivering optimized CPR and defibrillation therapy at the appropriate time has only recently become the focus of much clinical and basic science research worldwide.[15,16] The number of patients found in prolonged VF or a nonshockable rhythm such as pulseless electrical activity has increased significantly over the years. Therefore, treatment protocols must overcome this challenge to significantly impact on survival rates. This study highlights a number of potential physiologic indicators of VF duration, which could form part of a diagnostic algorithm to tackle the issue of delayed patient access leading to a prolonged cardiac arrest. Achieving a favorable outcome after prolonged out-of-hospital cardiac arrests could alleviate the burden on many hospitals of providing extended in-hospital pharmacologic and ventilation support. There is even some evidence that in-hospital pharmacologic interventions such as epinephrine can be detrimental to a cardiac arrest victim's long-term health, suggesting that endotoxemia could be consequence of prolonged cardiac arrest.[17,18]

This study shows that there is a direct correlation between the P-P interval and duration of VF ($r = 0.97$; mean correlation coefficient over 10 cases). The changes in P-P interval were gradual in comparison to the changes in EEG (BIS index) and dominant frequency of VF (hertz) over time during the cardiac arrest (VF). The change in these potential indicators appeared to be more gradual over the first 6 to 8 minutes and then decreased more sharply after 8 to 12 minutes (metabolic phase). The DA show that after 3 to 4 minutes of VF, the DA falls to less than 1.16 mV/sample. The graph also shows a steep decline after the electrical phase and then plateaus at the start of the metabolic phase. The changes in P-P interval have shown that there is a strong relationship between the changes in the electrical activity in the atria and the electrical activity in the ventricles within the myocardium during VF. There is also, as expected, at the initiation of the metabolic phase of cardiac arrest a steep decline in the model's BIS index (EEG).[19,20] Finally, the dominant frequency of VF that was previously demonstrated by Carlisle and colleagues[21] also decreases over time during prolonged VF, and again, the decline is more pronounced at the latter stages of the circulatory phase. DA also reinforces these findings and has the potential as a treatment protocol for out-of-hospital cardiac arrests.

As a result of the increasing number of bystander-witnessed arrests, the efforts are now focused on enhancing the diagnostic capabilities of automated external defibrillators. An increasing number of patients, because of the barrier of increased access times, are found to be in pulseless electrical activity or borderline fine VF. In response to these findings and the recommendations made by the European Resuscitation Council and American Heart Association in 2005,[22,23] a number of studies have attempted to address the challenge of accurately determining the duration of VF.[10-14] Callaway and Sherman have investigated parameters such as the frequency ratio and the scaling exponent, both of which our group has applied offline. However, the DA appears to be less costly in terms of processor power required.[10,11] In addition research groups are now applying the 3-phase time model, on which this research is based, to out-of-hospital treatment algorithms.[12]

If out-of-hospital treatment of cardiac arrest was optimized in terms of access times, CPR training, defibrillation performance, and post-resuscitative care, then the need for repetitive doses of drugs such epinephrine could perhaps be limited. Emphasis should instead be placed on advancing diagnostic algorithms, training, and the administration of lower-energy shocks to reduce the chances of myocardial dysfunction, thereby enhancing the patient's quality of life after the successful restoration of coronary stability.[24]

## Conclusion

The dominant frequency during VF, the DA, the P-P interval, and the BIS index are all potential physiologic indicators of VF duration. The findings from this study are innovative in terms of novelty and their potential applications. The changes in EEG during VF have potential applications for in-hospital vital signs defibrillation and ECG monitoring systems.

## Acknowledgment

We would like to thank the staff of the Lab Services Unit, Belfast, Northern Ireland, for their support during this study.

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