Real-time electrogram analysis for monitoring coronary blood flow during human ventricular fibrillation: Implications for CPR

Karthikeyan Umapathy, MD,* Farbod H. Foomany, MD, FHRS,* Paul Dorian, FHRS,[†] Talha Farid, MD,[‡] Gopal Sivagangabalan, MD,[‡] Krishnakumar Nair, MD,[‡] Stephane Masse, MD,[‡] Sridhar Krishnan, MD,* Kumaraswamy Nanthakumar, MD[‡]

*From *Ryerson University, [†]St. Michael's Hospital, and [‡]The Hull Family Cardiac Fibrillation Management Laboratory, Division of Cardiology, Toronto General Hospital, Toronto, Ontario, Canada.*

BACKGROUND Effective chest compressions during prolonged ventricular fibrillation (VF) have been shown to increase the chances of successful defibrillation to a rhythm associated with a sustainable cardiac output. There is currently no effective method of recording the degree of antegrade coronary artery flow during chest compression in VF.

OBJECTIVE This study sought to quantify the relationship between the antegrade coronary flow and the characteristics of human VF using near real-time wavelet-based electrocardiographic markers.

METHODS VF experiments were conducted in 8 isolated human hearts. The Langendorff perfusion enabled different flow rates (perfusion) during VF, which allowed for the simulation of chest compression with different efficacies. After the initiation of VF, the hearts were maintained in ischemia (no flow) for 3 minutes, followed by a 2-minute reperfusion and defibrillation. The experiments were repeated at flows of 0%, 30%, and 100% of baseline perfusion, and volume-conducted surface electrograms were recorded and analyzed using continuous wavelet transform in 5-second frames.

RESULTS Near real-time wavelet features were derived that demonstrated significant differences in the multicomponent nature of VF signals and predicted perfusion rate characteristics for different flow rates (i.e., 0%, 30%, and 100%; $P < .0006$). A pattern classifier was trained using the feature values from 5 hearts, and the flow rates for 3 additional hearts were predicted with an accuracy of 90%.

CONCLUSION VF electrogram characteristics as measured by wavelet analysis relate to antegrade coronary flow rate during VF. These findings suggest that chest compression efficacy of physiological importance could be monitored using near real-time wavelet analysis.

KEYWORDS Antegrade coronary flow; Cardiopulmonary resuscitation; Wavelet analysis; Human ventricular fibrillation

ABBREVIATIONS **AMSA** = amplitude spectral area; **CENTER** = scale with the highest energy in the distribution; **CF** = centroid frequency; **CPR** = cardiopulmonary resuscitation; **CWT** = continuous wavelet transform; **DF** = dominant frequency; **ECG** = electrocardiograph; **EMS** = emergency medical services; **ENTR** = entropy of the average energy distribution among scales; **LAC** = logarithm of the absolute correlations; **SDW** = scale distribution width; **SDW-U** = scale distribution width with uniform scale index; **SFM** = spectral flatness measure; **VF** = ventricular fibrillation

(Heart Rhythm 2011;8:740–749)

Introduction

Out-of-hospital cardiac arrests account for approximately 166,000 to 310,000 deaths in North America annually.[1] The only effective treatment for ventricular fibrillation (VF) is early defibrillation. The administration of chest compression during a prolonged episode of VF has been shown to improve return of spontaneous circulation in a canine model[2] and patient survival to discharge from hospital.[3] While effective cardiopulmonary resuscitation (CPR) that produces a good antegrade flow could increase the survival rate, ineffective CPR that produces poor antegrade flow could reduce the survival rate by delaying the shock treatment. Hence quantifying the efficacy of CPR (or the amount of antegrade coronary artery flow) and providing near real-time feedback to the emergency medical services (EMS) response team is of significant importance. Most reports on predicting the shock outcomes were performed on retrospective data and thus cannot evaluate the effect of different antegrade flow rates on electrocardiographic (ECG) characteristics.[3–6] Thus there still remains a knowledge gap in the literature in relating the CPR efficacy in terms of antegrade coronary flow and quantifiable ECG characteristics that could be useful in improving survival outcomes.

Drs. Umapathy and Foomany contributed equally to this work.

This study was supported by the Heart and Stroke Federation Fund Grant PG-07-0382 for optimizing CPR outcomes and Canadian Institutes of Health Research Grant MOP 777687 to Dr. Nanthakumar and Ryerson University. Dr. Nanthakumar is a recipient of the Clinician-Scientist Award from the Canadian Institutes of Health Research. **Address reprint requests and correspondence:** Dr. Kumaraswamy Nanthakumar, The Hull Family Cardiac Fibrillation Management Laboratory, Division of Cardiology, Toronto General Hospital, 200 Elizabeth Street, Gerrard Wing, 3-522b, Toronto, Ontario M5G 2C4, Canada. E-mail address: k.nanthakumar@uhn.on.ca. (Received August 9, 2010; accepted December 17, 2010)

1547-5271/$ -see front matter doi:10.1016/j.hrthm.2010.12.033

Brown et al[7,8] using median or centroid frequency (CF) and Eftestol et al[4] using spectral flatness measures (SFM) and band-limited energy were some of the first to evaluate prediction of defibrillation results. Watson et al[9] identified hidden structures in VF based on wavelet analysis. Callaway et al[10] proposed new chaos-based features for VF analysis such as scaling exponent for fractal self-similarity dimension, which shows how the signal is different from a pure random signal. Povoas et al[6] suggested the sum of the product of individual amplitudes and frequencies called amplitude spectral area (AMSA) as a prediction marker for defibrillation success. Watson et al[5,11] compared several global markers for predicting defibrillation success. Jagric et al[12] and Sherman et al[13,14] have utilized the approaches that quantified the irregularity and self-similarity of signal structures in predicting the success of defibrillation. We[15] introduced a scale distribution width (SDW) marker that measured the width of the distribution of wavelet energy among scales, thereby measuring the degree of organization or disorganization (or complexity) of VF signal.

All of the aforementioned works were performed on retrospective data with a main focus of predicting the end result of the shock rather than to quantify the efficacy of chest compressions or relate the antegrade flow rate to the electrical response of the heart. The knowledge gap in most of the existing studies is that it is not possible for these studies to establish whether CPR was effective in terms of antegrade flow. The reason for this major knowledge gap because it is not ethical to vary antegrade flow during VF in a living subject. The proposed study attempts to fill this knowledge gap by performing unique experiments on isolated human hearts in a Langendorff setup to determine the relationship between the varying amount of antegrade flow and the changes in VF electrograms by using wavelet analysis of the pseudosurface electrograms acquired during VF.

Methods

Data collection and experimental protocol

The study was performed using isolated human hearts; all patients with end-stage cardiomyopathy were included; patients with complex congenital cardiomyopathy were excluded. Langendorff perfusion was used for controlling antegrade flow coronary flows. The VF electrograms used in this study consisted of data from 8 isolated hearts that were perfused in a random fashion with 3 different perfusion rates. The pseudosurface ECG was sampled at 1 kHz during acquisition and down-sampled to 250 Hz for the analysis to reduce the computational complexity.

Immediately after the heart was explanted from the recipient, the human heart was placed in cold Tyrode solution and transported to an adjacent room. The right and left coronary arteries were cannulated and fitted to a Langendorff setup. The hearts were then Langendorff perfused with Tyrode solution (95% O_2 + 5% CO_2) at a 100% flow rate of 0.9 to 1.1 ml/g/min. Perfusion pressure was adjusted to maintain a pressure of 60 to 70 mm Hg. The entire isolated human heart was immersed in the temperature-controlled Tyrode solution. The temperature was maintained at 37°C and continuously monitored in the coronary sinus effluent such that it reflected myocardial temperature. During the isolated heart experiments, the epicardium may experience temperature differences compared with the endocardium. Hence, we monitored the temperature to ensure there was never a temperature differential greater than 0.25°C between the epicardium and endocardium.

The heart was paced at a cycle length of 600 ms to keep it perfused and functional. Before the induction of VF, pacing was stopped and VF was induced by making contact with the 2 poles of a 9-volt battery. After the initiation of VF, the hearts were maintained in ischemia (no flow) for 3 minutes, followed by a 2-minute reperfusion and defibrillation. The experiments were repeated for reperfusion rates of 0%, 30%, and 100% flow simulating chest compression with different efficacies. The reperfusion flows were continuous compared with the pulsatile (due to chest compression) in a real-world situation. The sequence of data acquisition for perfusion rates was randomized to minimize the time effect. Moreover, as will be explained later, we computed the electrical response of the heart during reperfusion relative to the corresponding ischemia stage or a standard reference, which eliminates the effects of time. Different perfusion rates (0%, 30%, and 100%) were achieved by controlling the flow with reference to the 100% flow measured in terms of pressure. Between experiments with different perfusion rates, the heart was perfused with 100% flow for 5 minutes to restore the heart from ischemic changes induced in the previous experiment. Figure 1 shows the details of the experiment protocol. A pseudosurface electrogram was recorded continuously for the 5-minute (3 minutes of ischemia and 2 minutes of reperfusion) duration. This protocol was approved by the University Health Network ethics committee, and informed consent was obtained from each of the patients.

Wavelet analysis

This method of wavelet analysis uses continuous wavelet transform (CWT). In CWT a signal $x(t)$ is modeled using all possible translated and dilated versions of a mother wavelet $\psi_{a,b}$ (i.e., a small waveform) where a and b are the dilational (or scale) and translational (or position) parameters. CWT can be mathematically expressed as:

$$CWT_x(a,b) = \frac{1}{\sqrt{a}}\int_{-\infty}^{\infty} x(t)\psi^*\left(\frac{t-b}{a}\right)dt$$

In this study $x(t)$ is the surface electrogram acquired during VF. Before decomposing the VF waveforms using wavelet analysis, a band pass filter (Butterworth 6 tap, 2 to 15 Hz) was applied to eliminate low- and high-frequency artifacts. Filtered VF electrograms were then segmented into 5-second (i.e., 1,250 samples at 250 Hz) segments to mimic a real-time acquisition with a buffer of 5-second data. Sequentially, each of the 5-second data were decomposed with an overlap of 50% using a range of wavelet scales