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The influence of myocardial substrate on ventricular fibrillation waveform: A swine model of acute and postmyocardial infarction

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Abstract

Objective—In cardiac arrest resulting from ventricular fibrillation, the ventricular fibrillation waveform may be a clue to its duration and predict the likelihood of shock success. However, ventricular fibrillation occurs in different myocardial substrates such as ischemia, heart failure, and structurally normal hearts. We hypothesized that ventricular fibrillation is altered by myocardial infarction and varies from the acute to postmyocardial infarction periods.

Design—An animal intervention study was conducted with comparison to a control group.

Setting—This study took place in a university animal laboratory.

Subjects—Study subjects included 37 swine.

Interventions—Myocardial infarction was induced by occlusion of the midleft anterior descending artery. Ventricular fibrillation was induced in control swine, acute myocardial infarction swine, and in postmyocardial infarction swine after a 2-wk recovery period.

Measurements and Main Results—Ventricular fibrillation was recorded in 11 swine with acute myocardial infarction, ten post-myocardial infarction, and 16 controls. Frequency (mean, median, dominant, and bandwidth) and amplitude-related content (slope, slope-amp [slope divided by amplitude], and amplitude-spectrum area) were analyzed. Frequencies at 5 mins of ventricular fibrillation were altered in both acute myocardial infarction ($p < .001$ for all frequency characteristics) and postmyocardial infarction swine ($p = .015$ for mean, $.002$ for median, $.002$ for dominant frequency, and $< .001$ for bandwidth). At 5 mins, median frequency was highest in controls, $10.9 \pm .4$ Hz; lowest in acute myocardial infarction, $8.4 \pm .5$ Hz; and intermediate in postmyocardial infarction, $9.7 \pm .5$ Hz ($p < .001$ for acute myocardial infarction and $p = .002$ for postmyocardial infarction compared with control). Slope and amplitude-spectrum area were similar among the three groups with a shallow decline after minute 2, whereas slope-amp remained significantly altered for acute myocardial infarction swine at 5 mins ($p = .003$).

Conclusions—Ventricular fibrillation frequencies depend on myocardial substrate and evolve from the acute through healing phases of myocardial infarction. Amplitude related measures,

however, are similar among these groups. It is unknown how defibrillation may be affected by relying on the ventricular fibrillation waveform without considering myocardial substrate.

Keywords

myocardial infarction; cardiopulmonary resuscitation; heart arrest; defibrillation; ventricular fibrillation; sudden cardiac death

Over 60% of cardiac deaths are attributed to sudden cardiac death per year, with coronary heart disease as the underlying cause in 62% of sudden cardiac deaths (1). Sudden death, attributed to ventricular fibrillation (VF), remains an important cause of death in this country. Defibrillation by external patches delivered by an automated external defibrillator (AED) can restore a perfusing rhythm if delivered early in VF (2–4), but the likelihood of a shock resulting in pulse-less electrical activity or asystole increases with the duration of VF. In VF greater than 4 mins, as measured from the time when emergency medical services are called, chest compressions before the first defibrillation shock have been shown to improve survival in population studies in Seattle (5) and Norway (6). However, in many cardiac arrests, particularly if unwitnessed, the duration of VF is unknown to the paramedics who respond.

Therefore, there has been great interest in studying potential surrogates for VF duration. In animal models, certain parameters of the VF waveform vary with time and can predict a return of spontaneous circulation (ROSC) (7–10). Furthermore, the predictive capability of these waveform characteristics has been demonstrated in human studies as well (11–15). This has prompted the development of “smart” AEDs that will analyze the VF waveform and direct rescuers whether to shock or deliver chest compressions. However, it is unclear whether the waveform can predict the success of defibrillation to a ROSC better than, or independent of, the duration of VF.

Further complicating the design of a “smart” AED is that waveform characteristics may be different in different myocardial substrates. It has been previously demonstrated in rat and swine models that waveform characteristics were significantly altered compared with controls in heart failure resulting from myocardial infarction (16) as well as during an acute myocardial infarction (17,18). We therefore hypothesized that the VF waveform would also be altered after an acute myocardial infarction once a myocardial scar was present. This study compares VF waveform characteristics in three different myocardial substrates: acute myocardial infarction (acute MI), post-MI with scar (post-MI), and control.

METHODS

Experimental protocols were approved by the University of Arizona Institutional Animal Care and Use Committee. Domestic female swine were used in this study. All animals were subjected to anesthesia with an induction of 5% isoflurane in 100% oxygen delivered by a nose cone followed by oral endotracheal intubation. Mechanical ventilation was achieved with a rate- and volume-regulated ventilator (Narkomed 2A; North American Drager, Tel-ford, PA) on a mixture of room air and titrated isoflurane (1.5% to 3%). Initial ventilation was set at 12 respirations per minute with tidal volume of 15 mL/kg. Rate and tidal volume were adjusted to maintain an end-tidal P_{CO_2} of 40 ± 3 mm Hg. The lowest concentration of anesthetic that prevented movement during surgical instrumentation was used. Millar (MCP-500; Millar Instruments, Houston, TX) micromanometer-tip, solid state pressure transducers were placed in the descending aorta and right atrium. A fluid-filled Swan-Ganz catheter was placed in the pulmonary artery to record pulmonary capillary wedge pressure in the post-MI group. Correct catheter placement was verified by fluoroscopy. Measurements of electrocardiogram (ECG), right atrial pressure, and aortic pressure were continuously recorded (P3P Ponemah Physiology

Platform; Data Sciences International, St. Paul, MN). In the post-MI group, contrast ventriculography was performed before MI and again 2 wks later just before induction of VF to determine left ventricular ejection fraction. A pacing catheter electrode was placed into the right ventricle to induce VF with a 100-Hz alternating current. Ventricular fibrillation was confirmed by the ECG waveform and a precipitous decline in aortic pressure. Ventilation was discontinued and a continuous ECG was obtained for the duration of untreated VF. The control group consisted of normal animals that were not subjected to an MI but had VF induced in the same manner.

For animals in the acute MI group, an acute MI was induced by placement of a stainless steel plug in the midleft anterior descending artery, just proximal to the second diagonal branch, confirmed by fluoroscopy and angiography demonstrating complete occlusion. If VF did not occur spontaneously by 15 mins after plug placement or if the pig developed severe hypotension, VF was then induced by application of a 100-Hz alternating current through a pacing catheter in the right ventricle. This is a well-established animal model of VF cardiac arrest in the setting of acute MI (19–21). VF occurred spontaneously in one animal and in the remainder was induced electrically. Animals in the control and acute MI groups were additionally studied in a prior investigation (17).

For animals in the post-MI group, an acute MI was induced in a manner similar to that used for the acute MI group followed by a 2-wk recovery period. Like in the acute MI group, a stainless steel plug was placed in the midleft anterior descending artery. However, the plug was placed just after the second diagonal branch, because in pilot studies, the animal did not survive for the 2-wk recovery period if the plug was placed more proximally. Lidocaine was also administered (2 mg/kg) to avoid ventricular fibrillation during induction of the acute MI. VF did occur spontaneously in three animals (two animals at approximately 45 mins after plug placement), and all were successfully resuscitated. After the 2-wk recovery period, the animal was brought back to the laboratory and hemodynamic measurements were obtained (pulmonary capillary wedge pressure, right atrial and aortic pressure), and contrast ventriculography was performed. Ventricular fibrillation was then induced by application of a 100-Hz alternating current through a pacing catheter in the right ventricle. At the end of the experiment, the heart was removed and examined for evidence of myocardial scar formation.

Data Acquisition

Electrocardiograms were obtained in x, y, and z orthogonal axes using needle electrodes. The x-axis was horizontal (left–right) in the midthorax caudal to the shoulder. The y-axis was vertical with electrodes placed in the suprasternal notch and subxiphoid space, whereas the z-axis was in the anteroposterior dimension with electrodes over the midsternum and spine. The y-axis recordings were used for analysis. Signals were amplified and filtered to exclude <.3 Hz and >300 Hz (P511K; Grass Instruments, West Warwick, RI). Outputs from the amplifiers were digitized with 14-bit resolution at 2000 samples/sec (instruNet 100; GW Instruments, Cambridge, MA). Recordings were obtained for at least 5 mins and stored on a desktop computer for later analysis.

Data Analysis

Signals were analyzed using customized software. Fast Fourier transforms were obtained every second from overlapping 8,192 (4.1 secs) data segments. Frequency-based parameters were calculated between 4 and 20 Hz to eliminate both low- and high-frequency noise.

Mean, median, and dominant frequencies were determined for each 4.1-sec data segment. Mean frequency was defined as the sum, from 4 to 20 Hz, of the product of the fast Fourier transform frequency and its associated power divided by the total power in that segment. Dominant

frequency was the frequency with the highest measured power in the range from 4 to 20 Hz. Median frequency was that frequency for which the integrated signal power was one half the total integrated power from 4 to 20 Hz. The bandwidth was defined as the frequency interval that corresponded to the 25th to 75th percentile for total power from 4 to 20 Hz (that is, integral of power versus frequency). For each frequency variable, separate linear regression lines were computed every 30 secs and then a value for each variable was chosen as the midpoint of the regression line.

The amplitude–spectrum area (AMSA) (10) was also calculated. AMSA was calculated as the summed product of frequency and square root of power at that frequency from 4 to 20 Hz. The waveform slope was also obtained (12). In contrast to AMSA which is computed from the frequency domain of the signal, slope is computed from the time domain signal voltage, $x(t)$, as the median of the absolute value of differences in signal voltage at specified time intervals, Δt , over a total time interval of 4.1 secs:

$$\text{Slope}(\Delta t) = \text{median}_{\text{for } t \text{ over } 4.1 \text{ s}} \{ \text{abs}[x(t) - x(t - \Delta t)] \} / \Delta t$$

For small Δt (that is, $\Delta t \ll 1/\text{mean frequency}$), waveform slope represents the linearized change in signal voltage, x , in a time interval Δt . We set $\Delta t = 5$ msec. We also computed the slope divided by signal amplitude, slope-amp, where signal amplitude was computed as the square root of the average of power from 4 to 20 Hz. By dividing out the amplitude, slope-amp represents the relative change in signal amplitude over Δt .

VF waveform data are presented as mean $\pm$ SEM, and hemodynamic and baseline characteristics of animals is presented as mean $\pm$ SD. Differences in hemodynamic and baseline characteristic values among the three groups of swine were evaluated with a one-way analysis of variance with a Bonferroni correction for multiple comparisons. Differences in LV ejection fraction from pre- to postinfarction were assessed with a paired Student's t -test. The first 5 mins of VF were analyzed from both groups. The general mixed regression method using swine as a random effect was used to analyze differences between groups. Linear and higher-order polynomials were used to eliminate any trends in the residuals. This method, in which a random effect refers to a population that is randomly selected and not prespecified, is a generalized extension of the method of analysis of variance. The random effects method is needed to account for serial correlations resulting from observations made over time in the same animal and as such is a generalized form of a repeated-measures analysis of variance. However, the random-effects method further allows the handling of missing data points, which can occur if there are gaps in signal recording. The method of linear contrast was then used to compare differences based on the random effects model (22) at specific time points. Linear contrast tests for differences at a point in time based on the computed regression coefficients from the random-effects model. Minutes 3 and 5 were assessed with a Bonferroni correction for multiple comparisons. Statistical testing was performed using Stata (College Station, TX) with significance set at $p < .05$.

RESULTS

A total of 11 acute MI, ten post-MI, and 16 control swine were studied. Baseline characteristics are given in Table 1. The weight of post-MI swine (40 ± 5 kg) was significantly larger than control (23 ± 1 kg, $p < .001$) and acute MI (27 ± 3 kg, $p < .001$) swine as a result of the weight gained by the animals during the 2-wk recovery period. In the post-MI group, there were significant increases in aortic systolic and diastolic pressures compared with control and acute MI swine (Table 1). However, LV ejection fraction was not significantly decreased: $54 \pm 10\%$

to $49 \pm 11\%$ ($p =$ not significant). In the post-MI group, visual inspection of the explanted heart showed the presence of an anterior–apical infarction with scar formation (Fig. 1).

Frequency characteristics were varied in the three swine groups (Fig. 2). In post-MI swine, we found significantly altered frequency characteristics compared with control swine. Time evolution as determined by general mixed regression was significantly altered in post-MI swine compared with controls for median frequency ($p = .006$) and dominant frequency ($p < .002$), although not for mean frequency; bandwidth was constantly depressed in post-MI swine throughout time ($p < .001$). At 3 and 5 mins of VF, post-MI swine showed significant differences compared with controls in median and dominant frequency and bandwidth (Table 2). Additionally, at 5 mins, mean frequency was altered in post-MI swine.

Time evolution as determined by a general mixed regression was significantly altered in acute MI swine compared with controls in mean ($p < .001$), median ($p < .001$), dominant frequency ($p < .001$), and bandwidth ($p < .001$). At both 3 and 5 mins, there were significant differences in mean, median, and dominant frequencies and bandwidth in acute MI compared with control animals (Table 2). There were no significant differences at 3 mins and 5 mins in any frequency parameters between acute MI and post-MI swine.

In contrast, the amplitude-related measures of AMSA and slope were similar among the three groups of swine (Fig. 3). AMSA decreased from mean values of approximately 80 to 100 mV Hz in the first minute to approximately 50–70 mV Hz by minute 2 with a slower decline through minute 5 to approximately 50 mV Hz (Fig. 3). Slope showed a similar overall time course, starting at approximately 4 mV/sec in the first minute and with a shallow decline from minutes 2 to 5 reaching approximately 2.2 mV/sec. Although time evolution as assessed by the general regression method was altered for acute MI swine ($p < .001$ for AMSA and $p = .005$ for slope) and for post-MI swine for slope ($p = .04$), there were no significant differences at any time point in the first 5 mins between any swine group. With slope divided by amplitude, slope-amp, we found a significant difference in time evolution ($p < .001$) for acute MI swine compared with control (Fig. 3), but for which there was only a significant difference at 5 mins ($p = .003$). Slope-amp showed a time evolution that was similar to that seen in the frequency characteristics (mean, median, and dominant). Namely, there was an early dip at around 2 mins followed by a rise and plateau to minute 5.

DISCUSSION

This study has investigated the time evolution of the VF waveform during the first 5 mins in three myocardial substrates: acute MI, post-MI with scar, and control. These data establish that the VF waveform varies with different myocardial substrates. Specifically, the VF waveform shows different frequency properties in these three myocardial substrates, and by 5 mins, frequencies are lowest in an acute MI, highest in control, and intermediate in the post-MI state. However, the waveform measures that incorporate amplitude either in the frequency domain (AMSA) or time domain (slope) signal did not distinguish between the three substrates in the first 5 mins.

Slope-amp showed a time evolution that was similar to mean, median, and dominant frequencies. Slope-amp is a combination characteristic that divides the slope, computed from the time domain signal, by the amplitude (computed from the power spectrum from 2 to 20 Hz). AMSA, which is computed entirely from the frequency domain signal, is mathematically related to the mean frequency times the amplitude. Therefore, slope can be thought of as a “time domain” equivalent to AMSA, because when slope is divided by amplitude, one extracts what is in essence related to the mean frequency.

A variety of myocardial substrates are involved in the generation of ventricular fibrillation and cardiac arrest. These substrates include myocardial ischemia resulting from coronary artery disease, systolic heart failure as well as electrical diseases in a structurally normal heart such as long QT syndrome and Brugada syndrome. Although it is now recommended that patients with severe systolic heart failure undergo implantation of an implantable cardioverter defibrillator for prevention of sudden death (23), it is acknowledged that 50% of sudden deaths resulting from heart disease occur in low-risk patients who would not have been considered as candidates for an implantable cardioverter defibrillator as primary prevention (23,24), namely patients with ischemic heart disease but without heart failure. This study uses the clinically relevant model of MI in both acute and postinfarct stages and likely with different sizes of infarcted myocardial territory, because swine in the post-MI group had a midleft anterior descending occlusion and the acute MI group had a proximal left anterior descending artery occlusion. Furthermore, we did not induce systolic heart failure with MI, because LV function was not significantly altered from baseline ($54 \pm 10\%$ preinfarction to $49 \pm 11\%$ postinfarction, $p = \text{not significant}$). This swine MI model thus illustrates that chronic ischemic heart disease, even in the absence of systolic heart failure, also leads to altered waveform characteristics. The frequency characteristics of the VF waveform are known to be influenced by the metabolic milieu (25), and we speculate that an abnormal metabolic state may underlie the alterations in frequency that we have found in these abnormal myocardial substrates.

It has been well known that VF evolves over time from a coarse-appearing waveform to a fine-appearing waveform. Methods to quantify this visual impression by calculating frequencies and amplitudes were then developed over the past decade. Subsequently, studies of out-of-hospital cardiac arrest showed that survival was improved by chest compressions before a shock for VF of duration greater than 4 mins (5,6). These studies established the rationale that chest compressions in prolonged VF are necessary to improve the likelihood of successful defibrillation to ROSC and was based on the concepts that the pathophysiology of VF has distinct phases (26). In the electrical phase, which is during early VF, defibrillation should be performed and chest compressions are unlikely to improve the success of a shock to achieve immediate ROSC. The circulatory phase follows during which chest compressions are beneficial in readying the heart for defibrillation. Finally, in the metabolic phase, there is severe brain and cardiac injury and cardiopulmonary resuscitation is less beneficial. A retrospective analysis of out-of-hospital VF arrest suggested that the electrical phase lasts 5 mins, in which chest compressions before defibrillation are not beneficial (27).

Although these population studies established the relationship of VF duration and defibrillation success to achieve ROSC, it was also acknowledged that VF duration may be unknown, particularly if the collapse is not witnessed. Quantification of the VF waveform by characteristics such as frequency and amplitude then became viewed as a possible surrogate for time duration. Studies of the VF waveform in cardiac arrest have in fact demonstrated the power of the VF waveform to predict the success of a defibrillatory shock to achieve ROSC. In particular, higher frequency content has been known to be associated with a higher success of defibrillation (11,14,15,28). Furthermore, the parameters of AMSA and slope can predict successful shocks with a high sensitivity ($>90\%$) for identifying VF that is shockable to ROSC (12,13). Although this high sensitivity would imply that the VF waveform can serve as a surrogate for VF duration, this was investigated in a cohort of 40 patients sustaining cardiac arrest with the finding that waveform features did not correlate with time in VF (29). It may, in fact, be the VF waveform that is the key predictor of a successful shock to ROSC and not time itself. The implication of these concepts is that the electrical and circulatory phases of VF arrest are best identified based on VF waveform and not by time.

Despite the high sensitivity of waveform characteristics to predict a successful shock to achieve ROSC, the specificity of these parameters, including AMSA and slope, remains low at

approximately 50% (12,28,30). Thus, a large fraction of VF events that are not shockable to ROSC would be erroneously predicted to be shockable to ROSC based on an examination of the amplitude-based waveform characteristics. Furthermore, in an analysis of the rhythm before VF, it was found that slope was highest in patients in whom the preceding rhythm before VF was a perfusing one. However, in that situation, the slope was also similar, at approximately 5 mV/sec, between cases that were successfully shocked and those that were not successfully shocked to ROSC (31); thus, slope was not a specific predictor of ROSC in patients whose rhythm before VF was a perfusing one. We have demonstrated that VF frequencies are affected by myocardial substrate, whereas measures that incorporate amplitude information such as AMSA and slope are not affected by myocardial substrate. This equivalence in different substrates may seem to be an advantage to AMSA and slope. However, we speculate that the poor specificity of these parameters in human studies may be precisely the result of the failure of these amplitude-related measures to distinguish different myocardial substrates. That is, some patients with “good” amplitude-related measures (that is, suggestive of short-duration VF and high likelihood of successful defibrillation) may have had poor outcomes because of an associated acute MI. Additionally, the lack of correlation between VF waveform and VF duration observed in a human cardiac arrest cohort (29) may have been related to varied myocardial substrates that were not accounted for. If we ultimately adopt the strategy that waveform is a better predictor of defibrillation success to ROSC than VF duration, then we must be sure that such decision algorithms have been adequately investigated for the effect of the underlying myocardial substrate that is fibrillating.

Limitations

It is well known that waveform characteristics of VF in swine are different from those characteristics in humans. Ultimately, the effect of myocardial substrate on VF waveform will need to be investigated in human VF. However, such data are difficult to collect in population studies, particularly for patients who do not survive to hospital admission. Nonetheless, the observations in this study as well as in the rat model of heart failure resulting from MI (16) establish the effect of myocardial substrate on VF waveform characteristics and that this feature is not unique to one species of animal.

It is also a limitation that the animals in the post-MI group were significantly heavier than the controls and acute MI swine as a result of the 2-wk convalescence period, in which the animals grow at an expected rate for swine. The difference in weight may account for the small changes in hemodynamic parameters but is not likely to explain the changes in frequency characteristics. We have previously examined frequency characteristics in 4-kg, 14-kg, and 24-kg pigs and found frequencies to be mildly elevated in 14-kg animals, but without any significant differences between 4-kg and 24-kg animals (32). Importantly, we did not observe any differences in VF amplitude in the present study despite the weight differences.

This experimental design was not intended to define the relationships among myocardial substrate, VF waveform, and the likelihood of successful defibrillation to immediate ROSC. Future studies should explore whether waveform characteristics can predict defibrillation success independent of VF duration and whether such predictors are affected by myocardial substrate. Perhaps the transition from an electrical to circulatory phase of VF may be affected by substrate, and the ability to detect this transition by an examination of the waveform such as by AMSA slope, or slope-amp may also be affected by substrate. These are important issues that merit further investigation in both animal and population studies. If waveform predictors of resuscitation to a perfusing rhythm are affected by myocardial substrate, then strategies to incorporate this information quickly and efficiently at the rescue scene may be needed.

CONCLUSIONS

Waveform frequency characteristics of ventricular fibrillation are dependent on myocardial substrate during the first 5 mins, and these characteristics continue to evolve from the acute MI state through the postinfarction phase. Amplitude-related measures of AMSA and slope do not distinguish different myocardial substrates and show a flattened time response beyond the first 2 mins. It is unknown whether myocardial substrate alters the prediction of a successful defibrillation to a perfusing rhythm based on an examination of the VF waveform.

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Figure 1.
Explanted heart from a swine that was 2 wks from acute myocardial infarction. An anterior–apical scar is visible (*arrows*).

Figure 2.

Frequency characteristics of the ventricular fibrillation waveform for control ($n = 16$), acute myocardial infarction (MI) ($n = 11$), and post- MI ($n = 10$) swine. Mean (A), median (B), and dominant (C) frequencies are significantly altered among the three types of myocardial substrates, with post- MI swine showing frequencies beyond minute 3 that are intermediate between acute MI and control animals. Bandwidth (D) is also significantly altered, with post- MI animals showing the narrowest frequency bandwidth ($p < .001$ for overall time course differences for all frequency characteristics).

Figure 3.

Amplitude-based waveform characteristics of amplitude-spectrum area (AMSA) (A) and slope (B) are illustrated for swine among the three myocardial substrates of control ($n = 16$), acute myocardial infarction (MI) ($n = 11$), and post-MI ($n = 10$). In contrast to frequency characteristics, AMSA and slope are similar among the three groups of animals with an early sharp decrease in the first 2 mins followed by a shallow decline thereafter. In contrast, dividing slope by amplitude, slope-amp (C), unmasks the differences among the three groups ($p < .001$ for overall time course differences in slope-amp). MI, myocardial infarction.

Table 1

Baseline and hemodynamic characteristics

Group	Weight (kg)	HR (bpm)	Aortic Systolic Pressure (mm Hg)	Aortic Diastolic Pressure (mm Hg)	RA Pressure (mm Hg)	PCW (mm Hg)	Pre-Infarct LVEF (%)	Post-Infarct LVEF (%)
Control (N = 16)	22.7 ± 1.4	115 ± 17	71 ± 10	46 ± 7	6 ± 1			
Acute MI (N = 11)	26.6 ± 2.6 ^a	107 ± 11	73 ± 16	46.7 ± 9.6	6 ± 1			
Post-MI (N = 10)	40 ± 5 ^b	98 ± 15 ^d	87 ± 10 ^c	64 ± 8 ^b	8 ± 4 ^d	12 ± 9	54 ± 10	49 ± 11

HR, heart rate; bpm, beats per minute; MI, myocardial infarction; RA, right atrial; PCW, pulmonary capillary wedge pressure; LVEF, left ventricular ejection fraction.

^a $p = .004$ for comparison of acute MI to control;

^b $p < .001$ for comparison of post-MI to control and to acute MI;

^c $p = .001$ for comparison of post-MI to control, and $p = .007$ for post-MI to acute MI;

^d $p = .02$ for comparison of post-MI to control.

Table 2
Frequency characteristics at 3 and 5 minutes of ventricular fibrillation

	Mean		Median		Dominant		Bandwidth	
	3 mins	5 mins	3 mins	5 mins	3 mins	5 mins	3 mins	5 mins
Control	9.5 ± 0.5 Hz	10.5 ± 0.4 Hz	9.7 ± 0.5 Hz	10.9 ± 0.4 Hz	9.3 ± 0.6 Hz	10.9 ± 0.6 Hz	3.0 ± 0.2 Hz	3.6 ± 0.2 Hz
Acute MI (<i>p</i> value relative to control) ^a	8.3 ± 0.4 Hz (<i>p</i> < .019)	8.3 ± 0.2 Hz (<i>p</i> < .001)	8.4 ± 0.5 Hz (<i>p</i> = .011)	8.4 ± 0.5 Hz (<i>p</i> < .001)	8.0 ± 0.6 Hz (<i>p</i> = .014)	7.9 ± 0.6 Hz (<i>p</i> < .001)	1.9 ± 0.2 Hz (<i>p</i> = .012)	2.9 ± 0.2 Hz (<i>p</i> < .001)
Post-MI (<i>p</i> value relative to control) ^a	8.1 ± 0.4 Hz (<i>p</i> = NS)	9.7 ± 0.4 Hz (<i>p</i> = .015)	7.9 ± 0.4 Hz (<i>p</i> = .009)	9.7 ± 0.5 Hz (<i>p</i> = .002)	7.3 ± 0.5 Hz (<i>p</i> = .012)	9.2 ± 0.6 Hz (<i>p</i> = .002)	1.9 ± 0.2 Hz (<i>p</i> < .001)	2.5 ± 0.2 Hz (<i>p</i> < .001)

^aThere were no significant differences at 3 mins and 5 mins in any frequency characteristic between acute MI and post-MI swine. MI, myocardial infarction.