HEART RATE RECOVERY FOLLOWING EXERCISE: A PREDICTOR OF VENTRICULAR FIBRILLATION SUSCEPTIBILITY AFTER MYOCARDIAL INFARCTION

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Abstract

Heart rate recovery (HRR) after exercise, thought to be related to cardiac parasympathetic tone, has been shown to be a prognostic tool for all-cause mortality. However, the relationship between this variable and confirmed susceptibility to ventricular fibrillation (VF) has not been established. Therefore, myocardial ischemia was induced by a 2 min occlusion of the left circumflex artery during the last min of exercise in mongrel dogs with myocardial infarction (n=105). Ventricular fibrillation was induced in 66 (S, susceptible) animals while the remaining 39 dogs had no arrhythmias (R, resistant). On a previous day, ECG was recorded and time series analysis of heart rate variability (HRV) was measured 30, 60, and 120 s after submaximal exercise (treadmill running). The HRR was significantly greater in resistant dogs than in susceptible dogs at all three times, with the most dramatic difference at the 30 s mark (R=48.1 ± 3.6, S=31.0 ± 2.2 beats per minute, change from maximum). Correspondingly, indices of parasympathetic tone increased to a significantly greater extent in resistant dogs at 30 s and 60 s post-exercise. These differences were eliminated by atropine pre-treatment. When considered together, these data suggest that resistant animals exhibit a more rapid recovery of vagal activity after exercise than those susceptible to VF. As such, post-exercise HRR may help identify patients with a high risk for VF following myocardial infarction.

Keywords: Cardiac parasympathetic tone; heart rate variability; sudden-death; arrhythmia risk
**Introduction**

Heart rate recovery after exercise has been shown to be an independent predictor of mortality across substantial and diverse population groups (11, 12, 13, 31, 34, 41, 47) with minimal exception (21). For example, Cole et al. (12) demonstrated in a multicenter study of 5,234 individuals that abnormal heart rate recovery after submaximal exercise predicts death, even after adjustment for various cofounders; Nishime et al. (34) published similar results from a total of 9,454 patients. Subsequent investigations have established that low heart rate recovery is linked to attenuated parasympathetic reactivation following the termination of exercise (1, 11, 12, 13, 25, 35, 37). Despite the large number of studies that examine heart rate recovery, the application of heart rate recovery data for patients recovering from myocardial infarction (MI), a population known to be at risk for sudden death, is sparse.

Numerous studies have suggested that, in MI survivors, heightened parasympathetic activity protects against ventricular fibrillation (4, 8, 10, 28), or that attenuated parasympathetic tone indicates a high risk for sudden cardiac death (29, 34, 40, 45). For instance, the ATRAMI trial (29), a multicenter study that examined 1,284 patients with recent myocardial infarction, established that autonomic tone is a strong independent indicator of mortality risk, and information from autonomic markers significantly increases prognostic ability. For several years, assorted measures of heart rate variability (HRV), an established index of cardiac parasympathetic activity, have been used to evaluate parasympathetic tone in patients with cardiovascular disease. It has been well established that low HRV, typically measured over a 24-hour period, is a marker of high arrhythmia risk in post-MI subjects (2, 19, 23, 27, 29, 41, 45). Yet there is room for criticism of this method, as it requires hand-editing of ectopic beats that can
be quite common in MI patients; there is no consensus on the best HRV measure to use, and standardization of commercial systems is lacking (24).

Because of these findings, it seems reasonable that heart rate recovery may offer additional insight into the parasympathetic function of MI patients and, therefore, the risk for malignant arrhythmias. Heart rate recovery is a more straightforward and easily obtained measurement compared to HRV and other indices of cardiac vagal tone, as it requires less time for data collection and fewer data processing algorithms. Additionally, heart rate recovery may show the vagal reactivity necessary for combating ventricular fibrillation during ischemic or other stress conditions when irregular heart rhythm could potentially occur. In a pioneering study, Nissinen et al. (33) examined heart rate recovery among survivors of acute MI and found it to be a more powerful predictor of all-cause mortality than traditional autonomic markers. However, the specific relationship of heart rate recovery following exercise and a confirmed susceptibility to lethal cardiac arrhythmias remains to be determined.

It was, therefore, the purpose of this study to investigate the relationship between heart rate recovery, cardiac parasympathetic activity, and susceptibility to malignant arrhythmias. In particular, the hypothesis that attenuated cardiac parasympathetic reactivation with the corresponding decline in heart rate recovery following exercise would be associated with an increased risk for ventricular fibrillation was tested. Time series analysis of heart rate variability, with and without atropine pretreatment, was used to evaluate cardiac parasympathetic reactivation in dogs with healed myocardial infarction that were subsequently found to be either susceptible or resistant to ventricular fibrillation.
Methods

Archived data from 105 (56 female and 47 male, weight 18.2 ± 0.4 kg) heartworm-free purpose-bred mongrel dogs (Kaiser Lake Kennels, Kaiser Lake, OH and Covance Research Products, Cumberland, VA) judged to be less than a year old by inspection of the teeth and the presence of the thymus gland at the time of surgery were used in this study. A consecutive sequence of animals in which a high quality ECG signal was recorded throughout the submaximal exercise test was selected. In a subset of these animals (n= 23), the submaximal exercise test was also performed after treatment with atropine sulfate. In some animals (n= 18), the heart rate recovery was evaluated during a second control exercise test recorded within one week of the first. The principles governing the care and treatment of animals as expressed by the American Physiological Society were followed at all times during this study. In addition, the Ohio State University Institutional Animal Care and Use Committee approved the procedures used in this study.

Surgical preparation of the canine model

The surgical preparation of the dogs has been described in previous publications (4, 5, 6, 40). Briefly, the dogs were anesthetized and, using strict aseptic techniques, a left thoracotomy was made in the fourth intercostal space. The heart was exposed and supported by a pericardial cradle. A hydraulic occluder and a 20-MHz Doppler flow transducer were placed around the left circumflex coronary artery. Insulated silver-coated copper wires were sutured to the epicardial surface of the left and right ventricle for later use in recording a ventricular electrogram. The left anterior coronary artery was ligated, producing an anterior-wall myocardial infarction. All leads to the
instrumentation were tunneled under the skin to exit at the back of the neck. Dogs were medicated to control postoperative pain and infection as described previously (4, 5).

**Exercise protocol**

Three to four weeks after surgery, the animals were trained to walk on a motor-driven treadmill for several days to familiarize them with the laboratory. Pre-exercise values of all the variables were obtained while the animals were standing on the treadmill before the onset of the running. The response to exercise was then assessed using a submaximal exercise protocol previously described by Tipton et al. (44), and as modified by Stone (42). Briefly, the treadmill exercise lasted a total of 18 min and was divided into 3 min blocks. The protocol began with a 3 min warm-up period during which the animal ran at 4.8 km/hr, 0% grade. The speed was increased to 6.4 km/hr and the grade of the treadmill was increased every 3 min as follows: 0, 4, 8, 12, 16%. In agreement with previous studies (5, 6, 42, 44), heart rate increased to approximately 70% (~210 beats per minute) of the maximum canine heart rate (46) during the last 3 min of exercise in the dogs included in the present study. After the completion of 18 min of exercise, the treadmill was stopped, and the animal remained standing while post-exercise ECG was obtained.

The effects of atropine were examined in a subsequent submaximal exercise test to evaluate the role of the parasympathetic nervous system. In the atropine subgroup of dogs, on a later day, a catheter was percutaneously placed in a cephalic vein so that atropine sulfate (50 µg/kg, American Pharmaceutical Partners, Schaumberg, IL) could be administered while the animal was running, approximately 2-3 minutes before the treadmill was stopped (i.e., when a new steady state heart rate had been achieved).
Susceptibility Classification: Exercise Plus Ischemia test

On a subsequent day (after completion of the submaximal exercise studies), exercise plus ischemia testing was used to classify the animals as either susceptible or resistant to ventricular fibrillation. This convention of categorizing the animals has been used since the original study employing this canine exercise model was published in 1982 (6). Briefly, the exercise level was increased every 3 min in the same manner as the submaximal exercise protocol. During the last minute of exercise, the left circumflex coronary artery was occluded. The treadmill was then stopped, and the occlusion was maintained for an additional minute for a total occlusion time of 2 min. Metal plates (11 cm diameter) were placed across the animal’s chest so that electrical defibrillation could be achieved with minimal delay, but only after the animal was unconscious. Electrocardiogram was recorded throughout the test, and left circumflex coronary blood flow was measured to confirm that the coronary occlusion was complete.

Data Analysis

All data were recorded on a Gould model 2800S 8-channel chart recorder (Gould Inc., Cleveland, OH). A ventricular electrogram was recorded using the leads sutured to the epicardium, and heart rate was determined with a Gould biotachometer. Coronary blood flow was measured with a University of Iowa model 545C pulsed Doppler flowmeter (Iowa City, IA).

Heart rate data is reported as the average of a 30 second time interval. Heart rate was recorded for the last 30 sec of exercise, from cessation to 30 s post-exercise, from 30 s to 60 s post-exercise, and from 90 s to 120 s post-exercise. These average values are reported as times 0, 30, 60, and 120 s, respectively, and are in units of beats per minute.
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(bpm). The heart rate recovery is defined as the absolute difference between the average heart rate during the last 30 s of exercise and the average heart rate for the given time period.

An estimate of cardiac vagal tone index (VT) was obtained using a Delta-Biometrics vagal tone monitor triggering off the electrocardiogram R-R interval (Urbana-Champaign, IL). This device employs the time-series signal processing techniques as developed by Porges (38) to estimate the amplitude of respiratory sinus arrhythmia. Details of this analysis have been described previously (5). Similarly, the variance of the R-R intervals was recorded and transformed to its natural logarithm to normalize the distribution; it is expressed as standard deviation of the R-R interval (SDRR). Finally, the range, which is the difference between the longest and shortest R-R intervals within each 30-second time period, was also obtained.

The data were analyzed by a 2-factor (group×time) ANOVA for repeated measures. Since repeated measures ANOVA depends on the homogeneity of covariance (equal correlates between the treatments), this sphericity assumption was tested using Mauchley’s test. If the sphericity assumption was violated, then the F-ratio was corrected using Huynh-Feldt correction. When the F ratio exceeded a critical value of P<0.05, the means were compared using Tukey-Kramer multiple comparison test. Values are reported as mean ± standard error. Microsoft Excel (Microsoft Corporation, Redmond, WA) and NCSS statistical software (Jerry Hintze, Kaysville, UT) were used for data processing.
Results

Susceptibility Classification

The exercise plus ischemia tests induced ventricular fibrillation in 66 of the 105 animals, which were categorized as susceptible (S), while 39 did not develop arrhythmias and were categorized as resistant (R) to sudden death. There were no gender or weight differences between the two groups. The resistant dogs (18.4 ± 0.5 kg, range 14.1 – 26.2 kg) consisted of 21 females and 18 males, while the susceptible group (18.1 ± 0.4 kg, range 13.2 – 27.7 kg) was composed of 36 females and 30 males.

Pre-exercise Variables

Before the onset of exercise, there were no significant differences in any of the variables measured (heart rate, $S = 123.7 \pm 2.7$, $R = 125.9 \pm 2.7$ bpm; vagal tone index, $S = 6.9 \pm 0.2$, $R = 7.0 \pm 0.3$ ln ms$^2$; R-R interval range, $S = 320 \pm 24$, $R = 303 \pm 24$ ms; standard deviation of the R-R interval, $S = 74 \pm 7$, $R = 68 \pm 6$ ms).

Control Heart Rate Recovery Measures

The average heart rate and absolute change in heart rate for both groups are shown in Figure 1. A scatter plot for the change in heart rate following the cessation of exercise averaged over the first 30 s for each animals is displayed in figure 2. The maximum heart rate achieved during exercise did not differ between the susceptible and resistant groups (212.4 ± 3.3 and 212.1 ± 4.5 bpm, respectively). However, resistant animals clearly exhibited a more rapid heart rate recovery with significant differences between the two groups in absolute heart rate changes noted at the 30, 60, and 120 second times periods. There was also a significant (P<0.001) susceptibility group effect for the heart rate change.
**Cardiac Parasympathetic Indices**

The corresponding vagal activity is shown in Figure 3. The vagal tone index (VT) was reduced to nearly the same level during exercise for both groups (R= 1.8 ± 0.2-2 and S= 1.4 ± 0.2 ln ms²). Through recovery, however, resistant animals had a significantly higher vagal tone at 30 and 60 second measurements. The mean vagal tone began to equalize at the 120-second mark. Similarly, R-R interval range was the same for both groups during maximum exercise, but resistant animals showed significantly higher values at 30 and 60 seconds before achieving the same level with the susceptible animals at 120 seconds. Finally, the standard deviation of the R-R interval (SDRR) followed a similar trend, though the difference between groups was only significant at the 30-second measurement. Overall, the susceptibility group effect was significant for all three measures (VT: P= 0.009, Range: P= 0.016, SDRR: P= 0.019) and the susceptibility-time interaction was significant for R-R interval range and SDRR (P= 0.031 and P= 0.017, respectively) but not for the vagal tone index (P= 0.154).

**Heart Rate Recovery Following Atropine Treatment**

Of the 23 dogs used in the atropine subgroup, 14 were susceptible and 9 were resistant. The mean heart rate recovery results for the atropine subgroup of animals are shown in Figure 4. Heart rate was elevated overall for both the susceptible and resistant groups (231.4 ± 5.7 and 232.4 ± 6.8 bpm during exercise, respectively), but it still qualitatively displayed the same trend of exponential decline seen without parasympathetic blockade. Heart rate recovery was less than the control condition
overall, but more notably, the difference between susceptible and resistant animals was eliminated; (susceptibility group effect, P= 0.868).

*Cardiac Parasympathetic Indices Following Atropine Treatment*

Figure 5 displays the vagal activity in the atropine subgroup. All three measures were lower overall (for max VT, R= 0.2 ± 0.1 and S= 0.4 ± 0.1 ln ms²). More importantly, after atropine treatment, there were no longer any differences noted between the susceptible and the resistant animals in any of the three vagal indices at any given time. Overall, there were no significant susceptibility group or susceptibility group-time interactions for any of the three parameters.

*Comparisons Between Repeated Submaximal Exercise Tests. s*

In a subset of animals, the heart rate recovery and the vagal indices were compared on two different days. The two groups were combined (18 dogs total, 11 susceptible and 7 resistant). The response to the exercise was similar on each presentation. For example, the absolute change in heart rate during the first 30 s was 27.9 ± 3.5 for the first exercise test and 29.2 ± 3.6 bpm during the second exercise test. Similar responses were noted at both the 60 s (First trial 63.5 ± 3.8, Second trial 62.9 ± 3.0 bpm) and 120 s (First trial 66.8 ± 3.8, Second trial 66.1 ± 2.9 bpm) time points. When an analysis of variance was performed, there was no significant difference between days in any of the parameters measured. Furthermore, the average change in heart rate during the first 30 s following exercise varied by only 5.0 ± 10.3% (Coefficient of variation = 12.3%) between the first and second submaximal exercise tests.
Discussion

The major findings of this study were: (a) heart rate recovery after exercise was slower in animals susceptible to ventricular fibrillation than in animals resistant to malignant arrhythmias, (b) susceptible animals had an attenuated parasympathetic reactivation corresponding with the reduced heart rate recovery, and (c) the differences in heart rate recovery and cardiac vagal indices of the two groups were eliminated with administration of atropine. These data suggest that the post-infarction animals with attenuated heart rate recovery, that probably reflects a reduced reactivation of cardiac parasympathetic control following exercise, are also at a high risk for ventricular fibrillation induced by acute ischemia. To the best of our knowledge, this is the first study to demonstrate a specific relationship between heart rate recovery and a confirmed increased risk for ventricular fibrillation.

Numerous investigations suggest that heart rate recovery can predict all-cause mortality in general populations (11, 12, 13, 31, 34, 47). A limited number of the studies have shown the usefulness of heart rate recovery for subjects with myocardial infarction. For example, Cole et al. (11) also studied a subgroup of patients with coronary artery disease and found heart rate recovery to be predictive of death among these 225 individuals. Nissinen et al. (33) also found heart rate recovery to be a predictor of all-cause death in a group of 229 post-MI patients, even claiming that heart rate recovery was a more powerful predictor of death than traditional autonomic markers. In addition, heart rate recovery data were recently shown to enhance the prognostic power of SPECT imaging and other clinical variables in patients with myocardial infarction (3, 17), although Desai et al. (16) did not find this correlation. However, it must be emphasized once again that none of the aforementioned studies evaluated the relationship between
Heart rate recovery and an increased risk for lethal arrhythmias in either the general population or in patients with pre-existing cardiovascular disease.

**Heart Rate Recovery and Cardiac Autonomic Regulation**

Heart rate recovery has been shown to be a function of parasympathetic activity immediately after exercise (1, 11, 12, 25, 35, 37). For example, Imai et al. (25), using logarithmic transformation of heart rate recovery in humans after four different levels of exercise, found two linear components: initial rapid decrease and subsequent slow decrease. In agreement with the present study, the initial rapid decrease disappeared after the administration of atropine, suggesting that this component depends on vagal reactivation. Other studies further demonstrated that heart rate recovery correlates with heart rate variability immediately after exercise (26, 30). The present study confirms these findings, as it is clear that when susceptible animals were compared to resistant animals, impaired heart rate recovery corresponded with a reduced cardiac vagal recovery, and the difference between the groups was eliminated when parasympathetic activity was blocked by atropine.

According to Eckberg (18), reduced vagal activity following exercise is indicative of poor parasympathetic responsiveness to the abrupt pressure changes that occur following tachycardia that can lead to arrhythmia formation. As such, heart rate recovery may in fact be a superior marker of arrhythmia risk. In other words, it is an indicator of parasympathetic activity under dynamic rather than passive conditions, so the subject can be evaluated in a stress setting that would be more likely to provoke arrhythmias.

The contribution of the sympathetic nervous system to the heart rate recovery response is less clear. There is less certainty concerning the contribution of the
sympathetic nervous system to the heart rate recovery following exercise. Oleary (35) reported that sympathetic activity may undergo a sustained increase post-exercise which would tend to reduce the rate of heart rate recovery. In fact, Deferrari et al. (15) demonstrated that resistant animals often have weak cardiac sympathetic responses alone or in combination with powerful vagal reflexes. Furthermore, Taylor et al. (43) found that vagally-mediated heart rate responses are opposed by sympathetic stimulation at all breathing rates that they studied. Thus, it is possible that an elevated sympathetic stimulation following exercise in the susceptible animals could also contribute to the reduced heart rate recovery in these dogs. Indeed, an elevated sympathetic response may explain the higher heart rate in the susceptible animals noted at the 120 s time period, a time at which the various indices of cardiac parasympathetic activity have already equalized between the groups. However, any sympathetic contribution to the heart rate recovery differences is probably not large, as atropine eliminated the differences between the groups. One would predict that the inhibition of cardiac vagal activity would have allowed for the full expression of sympathetic effects and would thereby, exacerbate any heart rate differences due sympathetic activation. In the present study, both groups of animals exhibited a similar heart rate recovery following the atropine treatment. It therefore seems less likely that sympathetic activation contributed to the different heart rate recovery noted in the susceptible and resistant dogs. As sympathetic activation was not evaluated in the present study, a complete assessment of the potential role of altered sympathetic response to the attenuated heart rate recovery noted in the susceptible remains to be determined.
Limitations of the Study

In addition to the issue concerning the contribution of the sympathetic nervous system to the heart rate recovery, there are other limitations of the present study that should be considered. First, the best method of measuring heart rate recovery remains to be determined. Among previous studies, there is inconsistency in the type of exercise and recovery period. Additionally, heart rate recovery has been analyzed by the time elapsed before achieving a certain beats/min change (13) as a continuous variable of absolute change or percent change from exercise stop (11, 12, 26, 30, 32), as a categorical variable with varying cutoff points for abnormality (11, 12, 16, 17, 34, 41, 47), as an exponential decay model (25, 37, 39), or with more complex curve-fitting techniques (9, 25). In addition, there is no consensus as to the optimal time for monitoring heart rate post-exercise (48).

The current study utilized submaximal testing due to evidence that it is a more reliable alternative than maximal tests (25, 37). In the present study, heart rate recovery was analyzed as a continuous variable, as it is likely that the absolute value of the cutoff point in the dog would be different than that in man, due to the higher maximum heart rate in the former species. However, the cutoff point based upon the same percentage of maximum heart rate, is likely to be similar in both species. Additionally, heart rate recovery was evaluated as the absolute change for reasons of simplicity and to be consistent with related studies (26, 30). An exponential decay model was not considered because it has been shown to be ineffective in time periods of less than 3 minutes (37). Heart rate recovery measurements were limited to 120 seconds because it has been suggested that, during this two-minute window, heart rate recovery is primarily due to parasympathetic recovery, with minimal change in sympathetic activity (13, 25, 47).
regards to optimal time for measurement, the most dramatic difference between all
variables in the current study occurred at the 30 second mark after exercise, which is
consistent with the results by Imai et al. (25).

Second, a few authors have questioned the reproducibility of heart rate recovery
in a given individual (9, 48). In the present study, the heart rate recovery response was
very similar on separate days in the same animals. For example, the average change in
heart rate during the first 30 s following the cessation exercise varied by only 5.0 ± 10.2
% (coefficient of variation = 12.3%) between the first and second exercise test.. . Other
studies have also reported a similar level of reproducibility of the results when comparing
a limited number of individuals (7, 25).

Third, it should be acknowledged that in the present study, cardiac vagal tone was
only indirectly evaluated using various measures of heart rate variability. This study did
not measure the parasympathetic nerve activity directly. However, previous
investigations have verified that heart rate variability provides an accurate representation
of parasympathetic function (18). Additionally, in the current study, atropine effectively
eliminated the changes in both heart rate and the parasympathetic indices obtained by
time-series analysis. Therefore, it is reasonable to conclude that the method used in the
present study provided reliable indirect measurements of cardiac parasympathetic nerve
activity.

Finally, it is well established that that both respiratory rate and tidal volume can
alter heart rate variability (amplitude of the respiratory sinus arrhythmia)(22). As such,
differences in the respiratory response following exercise could indirectly contribute to
the differences in the cardiac vagal indices in the susceptible and resistant animals.
Respiratory parameters were not measured in this study due to the profound panting
response induced by exercise that continued throughout the post-exercise recovery period in both groups of animals. However, previous studies demonstrated that exercise elicited similar increases in respiratory rate in both susceptible and resistant animals (4). Furthermore, the vagal tone indices decreased to greater extent following beta-adrenergic receptor blockade, yet respiratory frequency increased to a similar extent after this intervention (4,5). These studies (4,5) also established that panting did not alter heart rate variability. Since both groups panted to a similar degree, it is unlikely that panting contributed significantly to heart rate recovery response differences noted in the susceptible and resistant animals.

There are some obstacles for the application of heart rate recovery to post-MI patients in a clinical setting due to the medications often prescribed. Patients recovering from MI typically receive beta-adrenergic receptor blocking drugs, which blunt the chronotropic response to exercise and could indirectly affect heart rate recovery (17). Other common drugs such as digitalis and angiotensin-converting enzyme inhibitors also have vagotonic actions (20, 22, 36) and could potentially heighten heart rate recovery so that it incorrectly denotes low-risk. Further study of the effect of these drugs on heart rate recovery in myocardial infarction patients is one of the many necessary steps toward clinical implementation of this new tool for evaluating ventricular fibrillation susceptibility.

In summary, the present study suggests that impaired heart rate recovery, measured as the absolute change in heart rate shortly after exercise cessation, is associated with high arrhythmia risk in dogs with healed myocardial infarction. The attenuated heart rate recovery seen in the animals subsequently shown to be susceptible to ventricular fibrillation almost certainly reflects reduced parasympathetic recovery after
exercise. Therefore, heart rate recovery following exercise can offer insight into the parasympathetic regulation of the heart under dynamic conditions similar to those that provoke arrhythmia formation. The present study further suggests that heart rate recovery after exercise may provide an additional marker of arrhythmia risk in patients surviving myocardial infarction.
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References


Figure Legends

**Figure 1.** Heart rate recovery following submaximal exercise in susceptible (n = 66) versus resistant (n = 39) animals. Top Panel: Heart rate at a given time period. Bottom Panel: The absolute difference in heart rate between the last 30 seconds of exercise and the time after the end of exercise as indicated. * P<0.01 susceptible versus resistant animals.

**Figure 2.** Scatter plot of the change in heart rate averaged over the first 30 s following exercise for each susceptible (n = 66) and each resistant (n = 39) dog. The mean ± standard error is also displayed for each group.

**Figure 3.** Indices of cardiac parasympathetic tone in susceptible (n = 66) versus resistant (n = 39) animals. A) Vagal tone index (R-R variability in the 0.24 to 1.04 Hz frequency range). B) R-R interval range (difference between the longest and the shortest R-R interval during a given 30 s interval). C) Standard deviation of the R-R interval for a given 30 s interval. * P<0.01 susceptible versus resistant animals.

**Figure 4.** The effects of atropine pre-treatment on heart rate recovery in susceptible (n = 14) versus resistant (n = 9) animals. Top Panel: Heart rate at a given time period. Bottom Panel: The absolute difference in heart rate between the last 30 seconds of
exercise and the time after the end of exercise as indicated. There were no significant differences between susceptible and resistant animals at any given time point.

**Figure 5.** The effect of atropine pre-treatment on indices of cardiac parasympathetic tone in susceptible (n = 14) versus resistant (n = 9) dogs after atropine administration A) Vagal tone index (R-R variability in the 0.24 to 1.04 Hz frequency range). B) R-R interval range (difference between the longest and the shortest R-R interval during a given 30 s interval). C) Standard deviation of the R-R interval for a given 30 s interval. Note that all variables are much lower values as compared to the control (no atropine) condition (see figure 2). There were no significant differences between susceptible and resistant animals at any given time point.
Figure 1.

Heart rate recovery for VF prediction post-MI
Figure 3.
Heart rate recovery for VF prediction post-MI

Figure 4

**Top graph:**
- **Y-axis:** Heart Rate (beats/min)
- **X-axis:** Time (s)
- **Legend:**
  - Susceptible
  - Resistant

**Bottom graph:**
- **Y-axis:** Heart Rate Recovery (beats/min)
- **X-axis:** Time (s)
- **Legend:**
  - Susceptible
  - Resistant
Figure 5.