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Observational Study of Human Electrical Muscle Incapacitation and Cardiac Effects

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Observational Study of Human Electrical Muscle Incapacitation and Cardiac Effects

John A. Gibbons, Andrew J, Mojica, Mark E. Peele, Brian B. Lupfer, Derrick F. Varner, Alan Ashworth

Human Electrical Muscular Incapacitation (HEMI) is used to subdue combative individuals. Changes in cardiac electrical activity have been proposed as the cause of death in a small fraction of these individuals. A study of 212 patient exposures to < 1000 volts found 28 (14%) developed QT prolongation. The current study sought to determine if changes in QTc interval occur after HEMI exposure. Twenty-four participants had EKG readings before a 5-second HEMI exposure and within 30 minutes after exposure. All subject EKGs were read by a data-blinded cardiac electrophysiologist who calculated a QT corrected (QTc) interval. QTc interval was calculated using Bazett, Fridericia, and Framingham methods. QTc prolongation was defined as >430 ms and a threshold of 30 ms for identifying QTc lengthening. Using the Bazett method, five participants experienced QTc prolongation and six had QTc lengthening. One participant developed QTc prolongation exceeding 500 ms, which carries a risk of developing multifocal ventricular tachycardia. These results suggest that HEMI exposure may cause EKG changes with a risk of ventricular tachycardia.
1.0 LIST OF FIGURES

Figure 1. Illustration of a single beat on an electrocardiogram
Figure 2. TASER X-26 output waveform
Figure 3. Individual subjects’ heart rate change
Figure 4. Individual subjects’ QTc change using Bazett method
Figure 5. Individual subjects’ QTc change using Fridericia method
Figure 6. Individual subjects’ QTc change using Framingham method
Figure 7. QT interval unadjusted for RR interval
Figure 8. QT interval after linear regression adjustment for RR interval
Figure 9. Individual subjects’ QTc change using Rubal method
Figure 10. Cardiac action potential
Figure 11. QT/RR and Rubal Method
2.0 LIST OF TABLES

Table 1. Descriptive statistics for mean heart rate and QTc interval
Table 2. Change in heart rate
Table 3. Change in QTc interval using Bazett method
Table 4. Change in QTc interval using Fridericia method
Table 5. Change in QTc interval using Framingham method
Table 6. Change in QTc interval using Rubal method
Table 7. Comparison of mean QT interval change calculation methods (n = 24)
Table 8. Magnitude of QTc exceeding thresholds (n = 24)
Table 9. QTc shortening versus QTc lengthening (n = 24)
Table 10. QTc lengthening exceeding thresholds (n = 24)
Table 11. Comparison of mean QT interval change calculation methods (n = 23)
Table 12. Magnitude of QTc exceeding thresholds (n = 23)
Table 13. QTc shortening versus QTc lengthening (n = 23)
Table 14. QTc lengthening exceeding thresholds (n = 23)
Table 15. Raw scores for RR Interval (sec), QT Interval (ms), QT/RR, Predicted QT/RR, and QTc (Rubal)
Table 16. Correlations (R²) between QTc and RR interval
### 3.0 LIST OF ACRONYMS

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tr>
<td>HEMI</td>
<td>Human Electrical Muscle Incapacitation</td>
</tr>
<tr>
<td>EKG</td>
<td>Electrocardiogram</td>
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<tr>
<td>TdP</td>
<td>Torsades de Pointes</td>
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<tr>
<td>TASER</td>
<td>Thomas A. Swift Electric Rifle</td>
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<td>HR</td>
<td>Heart Rate</td>
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<td>AFI</td>
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4.0 EXECUTIVE SUMMARY

Human electrical muscular incapacitation (HEMI) is widely used to subdue combative individuals. This study examined a possible effect of HEMI on electrical activity of the heart. Twenty-four active duty Security Forces personnel participating in TASER Instructor training volunteered to be subjects. All volunteers were screened for medical exclusions and provided written informed consent. A baseline electrocardiogram (EKG) was obtained before each HEMI exposure. The volunteers then experienced a five second HEMI exposure from an X-26 device. Within 30 minutes of the baseline EKG, a second EKG was obtained. A cardiac electrophysiologist read all of the EKGs without knowing the volunteer identification and before/after status of the EKG data.

The 48 EKGs were analyzed for RR interval, a measure of beat-to-beat heart rate, and QT interval, a measure of the time from initial contraction to relaxation of the heart ventricles. The QT interval was corrected for heart rate (QTc) by four different techniques. Two methods employed a logarithmic adjustment, including the Bazett and Fridericia methods. Two methods employed a linear regression adjustment, which were the Framingham and a novel method, referred to as Rubal for the individual who suggested this data analysis approach.

Overall findings showed a small lengthening in the QTc interval using the Rubal method. No significant change was found in mean heart rate or QTc interval using the Bazett, Fridericia, and Framingham methods. Visual inspection of the data suggested that there were two distinct groups, those whose QTc interval lengthened and those whose QTc interval shortened, with very few having no change. Highly significant changes were seen in these two groups using all four methods for QTc calculation. QTc lengthening reached the borderline threshold of a 30 ms increase for all but the Fridericia method, which showed a 28 ms increase. QTc interval lengthening exceeded 40 ms for about 25% of subjects using all four methods for QTc calculation and exceeded 60 ms for over 10% of subjects. One subject exceeded 500 ms, a threshold state with significant risk for developing ventricular fibrillation.

The results of this study show that significant lengthening of the QT interval can occur after a single 5-second HEMI exposure. Further research is needed to determine if QT interval lengthening is greater with multiple 5-second HEMI exposures, or if HEMI exposure and medications that are known to cause QTc prolongation have an interactive effect on this observed HEMI increase in QTc interval.
5.0 ACKNOWLEDGMENTS

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The views expressed are those of the authors and do not necessarily reflect those of the U.S. Government, U.S. Department of Defense, the U.S. Air Force, or the U.S. Army.
6.0 INTRODUCTION

Human Electrical Muscular Incapacitation (HEMI) is widely used by law enforcement officials to subdue combative individuals. A small fraction of these individuals subsequently die while in confinement. Critics of HEMI use claim these deaths are a direct effect of HEMI exposure. Changes in the electrical activity of the heart are frequently proposed as the cause. The electrocardiogram (ECG in Europe, EKG in the US) is a routine medical evaluation of cardiac electrical conductivity. Only a small number of human studies have examined EKG changes associated with HEMI exposure. Limitations in each of these studies leave some questions to be answered.

The objective of this study is to evaluate EKGs for electrical conductivity change after a controlled HEMI exposure, specifically investigating change in the QT interval.

Electrical shock has been reported to cause lengthening of the QT interval of an EKG. An Australian study of 212 low voltage (< 1000 volts) exposures found 28 (14%) patients developed QT prolongation, though only three patients had this change longer than six hours.\(^1\) The 14% incidence reported can be used as the upper limit for the effect size of electrical shock reported to cause QT prolongation. The following figure illustrates a full normal cardiac electrical cycle and labels the different segments. The QT interval represents the time from initial contraction to relaxation of the heart ventricles.

![Figure 1. Illustration electrical activity of a single heart beat on an electrocardiogram](image)

Prolonged QT interval can lead to development of ventricular tachycardia, in particular polymorphic ventricular tachycardia, also known as torsades de pointes (TdP). TdP may spontaneously revert to normal sinus rhythm or degrade to ventricular fibrillation with subsequent cardiac arrest. There is limited information in the published literature on the electrophysiological cardiac effects of HEMI exposure(s), particularly investigating ventricular electrical activity involving the QT interval.
An observational study of 105 volunteers undergoing HEMI exposure of 3.0 seconds mean interval (range 0.9 – 5 sec) reported volunteers developing both QT shortening and QT lengthening. Two published EKG strips document QT prolongation for a 2% incidence. This result can be used as a lower limit for the effect size of HEMI shown to cause QT prolongation. Limitations of this study were the use of only four limb leads, use of a single rhythm Lead II monitoring strip, and use of poor quality rhythm strips. QT interval should be assessed in multiple leads for accurate determination. This study likely underestimated the actual occurrence of QT prolongation.

In contrast, another study performed a series of 12-lead EKGs on 32 volunteers including before, immediately after, 16 hours after, and 24 hours after HEMI exposure. Thirty of the 32 baseline EKGs were reported as normal. The two volunteers with abnormal EKGs were noted to have the same findings at the three time points after HEMI exposure. No within subject comparison of before and after changes was performed, including QT interval. This second HEMI study was funded through a grant from TASER, International, and four of the listed authors were consultants for this firm. Though it is reassuring that no volunteer was found to develop absolute QT prolongation after HEMI exposure, it is possible that QT lengthening occurred but was not detected due to the absence of before and after comparisons. Also the sample size may have been too small to detect as small as a 2% incidence.

A third study of HEMI exposures obtained baseline 12-lead EKGs for 101 participants, either the day before or morning of exposure, and post-exposure EKGs, after at least 20 but not more than 22 hours. There were no significant mean changes in QT or heart rate-corrected QT (QTc) interval. Post-exposure QTc ranged from 380 to 442 ms. The major limitation of this study is that post-exposure EKGs were obtained 20-22 hours after exposure.

Clinically, the QT interval is corrected for heart rate (HR). Different methods are available to calculate QTc and different thresholds based on gender and age are used to define QT prolongation. Two nonlinear methods, Bazett and Fridericia, and two linear functions, Framingham and Hodges, are commonly used to adjust QT interval based upon heart rate. The Bazett and Fridericia methods were first proposed in 1920. These four methods are shown below.

\[
\begin{align*}
\text{Bazett} & \quad \text{QTc} = \frac{QT}{(HR/60)^{1/2}} \\
\text{Fridericia} & \quad \text{QTc} = \frac{QT}{(HR/60)^{1/3}} \\
\text{Framingham} & \quad \text{QTc} = QT + 154(1 - 60/HR) \\
\text{Hodges} & \quad \text{QTc} = QT + 1.75(60 - HR)
\end{align*}
\]

Congenital QT prolongation occurs in the U.S. population with prevalence estimates from 1/20,000 to 1/2,500. QTc prolongation can occur with medications as well. Several anti-arrhythmic drugs are recognized frequently to promote QT prolongation with subsequent development of TdP. This form of ventricular tachycardia can rapidly degenerate into...
ventricular fibrillation, with subsequent cardiac arrest. Conversely, torsades de pointes can spontaneously revert to normal sinus rhythm. Classes of medications reported to cause TdP include anti-arrhythmic medications, antipsychotic drugs, antidepressants (primarily tri-cyclic antidepressants), some antihistamines, antimicrobials (including erythromycin, clarithromycin, and ketoconazole), anti-malarial drugs (quineine and chloroquine), methadone, and cocaine.7,8,9

The Bazett method has been used to stratify the risk of developing TdP based upon QTc interval. The risk of cardiac events due to QTc lengthening is estimated as 1.052^x, where x is the increase QTc over 400 ms in multiples of 10 ms.10 For example, someone with a QTc of 440 ms has a 22% greater risk TdP development than someone with a QTc of 400 ms. A PubMed search was done using the term “risks of QT prolongation.” This search yielded 478 citations, but only a single published provided risk estimation involving QT prolongation. Data from congenital Long QT Syndrome studies indicates that QTc greater than 500 ms carries a 2-3 times higher risk for developing TdP.11 The Food and Drug Administration (FDA) requires pharmaceutical firms to provide QTc results using both the Bazett and Fridericia methods and provide both absolute QTc interval and change from baseline reported during new drug testing. Absolute QTc prolongation threshold values are > 450 ms, > 480 ms, and > 500 ms. QTc interval change from baseline value thresholds are 30 and 60 ms.12

QTc variability between EKGs was assessed in one study of 352 healthy subjects. Continuous Holter monitoring was used to record EKGs with subjects at rest during two separate sessions of 10 minutes in a supine position, during 10 minutes of unsupported sitting, and during 15 minutes of unsupported standing. The 95% confidence interval for supine QT variability was within ± 16 ms.13 This result is less than the FDA 30 ms threshold and the common clinical 40 ms threshold for QTc prolongation. Thus QTc variability between EKG tracings up to 45 minutes apart did not reach the threshold defined for QTc prolongation. Though not under investigation in the present study, lengthening of QT interval has been shown to be greater during sleep than wake state by 19 ± 7 ms.14

Data from Holter monitor recordings and 12-lead EKG cannot be compared. A study comparing Holter monitor uncorrected QT interval measurements with simultaneous 12-lead EKG found that lead V1 Holter monitor measurements ranged from 100 ms shorter to 55 ms longer, with a mean of 24 ms shorter, than EKG measurements. Lead V5 results showed that Holter monitor measurements ranged from 42 ms shorter to 62 ms longer, with a mean of 13 ms longer, than EKG measurements.15 This study did not capture data involving variability of QT interval over time.

Accurate interpretation of QT intervals has been shown to be dependent upon clinical expertise. A study showed two EKGs with congenital QT prolongation and two EKGs from healthy women to four groups of physicians: QT experts, arrhythmia experts, cardiologists, and non-cardiologists. QT intervals were correctly classified by 96% of QT experts, 62% of arrhythmia experts, and less than 25% of cardiologists or non-cardiologists.16 The limited availability of QT and arrhythmia experts has restricted QT interpretation of EKGs to the data analysis phase of HEMI studies.
In summary, there is scant information in the published literature on the cardiac electrophysiological effects of HEMI, particularly QT interval. The collection of before and after EKGs from volunteers undergoing controlled HEMI exposure permitted an assessment of the risk for QTc changes, a likely immediate event preceding serious injury and death associated with HEMI.
7.1 MATERIALS AND METHODS

7.2 Equipment


This device was used for all HEMI exposures. It is manufactured by TASER, International. It produces a timed burst of electrical pulses. It was operated in Probe Mode. Specific characteristics per the manufacturer are as follows.\textsuperscript{17}

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulse rate</td>
<td>16.5 to 20 pulses per second</td>
</tr>
<tr>
<td>Pulse duration</td>
<td>105 to 155 $\mu$sec</td>
</tr>
<tr>
<td>Peak load voltage</td>
<td>1,400 to 2,520 volts</td>
</tr>
<tr>
<td>Average current</td>
<td>1.5 to 2.4 mA</td>
</tr>
<tr>
<td>Energy delivered per pulse</td>
<td>0.095 to 0.125 joules</td>
</tr>
<tr>
<td>Power delivered into load</td>
<td>1.8 to 2.3 watts (= joules per second)</td>
</tr>
</tbody>
</table>

![Figure 2. TASER X-26 Output Waveform](image)

B. Electrocardiogram (EKG) machine – Burdick Atria 6100

This is an FDA approved medical office device. It was used in accordance with the approved indication to obtain and record 12-lead EKGs from participants. Date and time stamps were inserted on each EKG record. Participant number, rather than name or other identifying information, was entered as the patient name. Ten adhesive electrode pads were applied to the standard four limb and six precordial positions. EKG wires were attached between these electrode pads and the Burdick EKG machine to obtain a baseline 12-lead EKG for each participant. After obtaining a baseline EKG, the EKG wires were removed.
but the EKG electrode pads left in place. The same EKG electrode pads were used to obtain a post-exposure 12-lead EKG for each participant. This greatly reduced the time required to obtain a post-exposure EKG.

7.3 Subjects

A. The Active Shooter Incident Response Instructor training courses held at the USAF Security Forces Center, JBSA-Lackland TX, offer 5-second duration HEMI exposures to course participants. All participants are male or female USAF active duty, USAF Reserve, or Air National Guard personnel. All participants are on military orders to attend this course. Over 200 individuals are trained each year. Trainees in each class singly choose to or not to experience HEMI exposure. Every exposed volunteer signed an informed consent form before undergoing a training HEMI exposure.

B. This study enrolled volunteers only from attendees of Active Shooter Incident Response Instructor training courses who had already volunteered for HEMI exposure as part of their training. Twenty-two male and two female participants were recruited. Recruiting was performed through briefings to attendees at the start of the course. Participants received a 711 HPW/RHD Challenge Coin. The coins cost $12 each to purchase but have no monetary value.

C. Inclusion criteria

1. Male and female personnel 18-55 years of age
2. Participants in the Active Shooter Incident Response Instructor training courses, who had already given written consent for HEMI exposure as part of their training.
3. All participants must be fit for continued world-wide military service as defined in Chapter 5 of AFI 48-123 Medical Examinations and Standards.18

D. Exclusion criteria

1. Personnel with a medical waiver for continued military service.
2. A medical history or recent medication use that may confound the study results. See Appendix A, the Medical Screening Form, for the specific medical screening criteria used.
3. There exists the possibility of abnormal EKG findings that can be disqualifying for continued military service. Most of these conditions are symptomatic, meaning that an individual will know that this condition exists. Some conditions are disqualifying only if they interfere with the satisfactory performance of duty or place the individual at risk for sudden cardiac death. The other symptomatic conditions are indicative of underlying cardiac disease that requires medical management. In both situations, the affected individual is experiencing symptoms and should be under medical care for the relevant condition. The major unexpected risk to a military career is diagnosis of a prior silent heart attack, indicated by the presence of diagnostic Q waves on an EKG, and second degree Type II or third degree heart block, also known as high degree heart block.

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The Selvester QRS screening criteria, Appendix B, were used to identify Q-wave infarction. History of a silent heart attack and high degree heart block carry a risk of sudden cardiac death. Identifying individuals with such medical conditions actually provides a long-term benefit greater than the risk of disqualification for continued military service.

Appendix C lists heart conditions that are disqualifying for continued USAF military service. Comments on what the medical terms mean and the associated risks are included.

7.4 Data Collection Procedures

7.3.1 Baseline Pre-exposure EKGs

EKGs before HEMI exposure were obtained from all 24 volunteers. The pre-exposure 12-lead EKGs were obtained in the standard clinical manner with each participant at rest in the supine position. A unique three digit for each subject was the only identifying data entered into the EKG machine or printed on the EKG tracings. A portable examination table was used for the subjects to rest upon. Muscle artifacts were minimized by having each subject place both hands beneath the buttocks when recording data. After the baseline EKGs were recorded, the subjects then queued for HEMI exposure. The EKG electrode pads were left in place and used again for the post-exposure EKGs. All pre-exposure 12-lead EKGs were reviewed by Lt Col Gibbons, Maj Lupfer, or Maj Varner to ensure the absence of any disqualifying medical condition and data acquisition adequacy for interpretation before each participant was disconnected from the EKG machine. A privacy curtain and female chaperone were used when pre-exposure EKGs were obtained from the two female subjects.

7.3.2 HEMI Exposures

All subjects were recruited from students in the Active Shooter Incident Response Instructor training course offered by the Air Force Security Forces Center at JBSA-Lackland, TX. Each student received TASER, International, approved academic training on the bioeffects of HEMI. Students who underwent a HEMI exposure signed an informed consent document as part of the training course. A trained TASER, International, certified Master Instructor verified proper function of the X-26 device and operated the device for all subject exposures. Each subject was supported on either side by another student during the HEMI exposure to prevent an injurious fall. All exposures were done with the subject standing upon a padded sports mat. The X-26 electrodes were attached using alligator clips over the back of the left shoulder and over the back of the right iliac crest. The Master Instructor asked each subject if they were ready prior to starting a countdown to the HEMI exposure. A single 5-second HEMI exposure was delivered to each subject. The alligator clips were removed after the completion of each HEMI exposure.

7.3.3 Post-exposure EKGs
Post-exposure EKGs were obtained after the 5-second HEMI exposure and within 30 minutes of the pre-exposure EKG. The time between the pre- and post-exposure EKGs ranged from 7 minutes 34 seconds to 28 minutes 26 seconds, with a mean interval 15 minutes 34 seconds. Because the EKGs were collected on a non-interference basis with the course activities, it was not possible to control when any given subject was available for obtaining the post-exposure EKG. All post-exposure 12-lead EKGs were reviewed by Lt Col Gibbons, Maj Lupfer, or Maj Varner to ensure data adequacy for interpretation before each participant was disconnected from the EKG machine. After the post-exposure EKG recording was printed, the electrode pads were removed each subject. A privacy curtain and female chaperone were used when post-exposure EKGs were obtained from the two female subjects.

7.4 Data Analysis

All EKGs were read by a cardiac electrophysiologist who was blind to the identity of the subjects. RR interval and QT interval were measured for each of the 48 EKGs. QTc interval calculations were done using the Bazett, Fridericia, Framingham, and a novel linear method (Rubal) to adjust QT interval for heart rate variation.

Test data were analyzed using the open source statistics package R.
8.1 RESULTS

8.2 Descriptive Statistics

Heart rate and QT interval were measured before and after HEMI exposure. Four calculations were used to correct QT interval for heart rate: the Bazett, Fridericia, Framingham, and Rubal methods. Descriptive statistics for the heart rate and corrected QT interval are provided in Table 1.

Table 1

<table>
<thead>
<tr>
<th>QTc</th>
<th>M</th>
<th>Mdn</th>
<th>SD</th>
<th>Min</th>
<th>Max</th>
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<td>68</td>
<td>69</td>
<td>10.75</td>
<td>46</td>
<td>86</td>
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<tr>
<td>Post</td>
<td>68</td>
<td>68</td>
<td>13.03</td>
<td>43</td>
<td>93</td>
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<tr>
<td>Bazett</td>
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<tr>
<td>Pre</td>
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<td>390</td>
<td>30.67</td>
<td>342</td>
<td>452</td>
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<tr>
<td>Post</td>
<td>402</td>
<td>399</td>
<td>45.67</td>
<td>317</td>
<td>539</td>
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<tr>
<td>Fridericia</td>
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<tr>
<td>Pre</td>
<td>382</td>
<td>381</td>
<td>25.06</td>
<td>332</td>
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<tr>
<td>Post</td>
<td>394</td>
<td>392</td>
<td>35.73</td>
<td>327</td>
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<td>Framingham</td>
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<td>Pre</td>
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<tr>
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<td>37.28</td>
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<td>414</td>
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<tr>
<td>Post</td>
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<td>426</td>
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Note. M = Mean; Mdn = Median; SD = Standard Deviation.
### 8.3 Change in Heart Rate from Pre- to Post-Exposure

Table 2

*Change in Heart Rate (beats per minute)*

<table>
<thead>
<tr>
<th>Subject ID</th>
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</tr>
<tr>
<td>X</td>
<td>71</td>
<td>89</td>
<td>17</td>
</tr>
</tbody>
</table>

| Mean       | 68  | 68   | 0      |
Figure 3. Individual subjects’ heart rate change (units = beats per minute). Green dotted line represents decrease heart rate subjects (Pre > Post). Red solid line represents increase heart rate subjects (Pre < Post).

8.4 Change in QTc Interval Using the Bazett Method

The Bazett method is the most common method used in clinical studies for calculating the risk of cardiac events based on QTc interval. This method has been found to consistently over estimate QT intervals for heart rates above 60 beats per minute. It is one of two QTc calculation methods that the FDA requires when a pharmaceutical company submits data about drug effects on QT interval. It is included to provide comparison of these results with other studies.
Table 3

*Change in QTc Interval using Bazett Method (ms)*

<table>
<thead>
<tr>
<th>Subject ID</th>
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<th>Post</th>
<th>Change</th>
</tr>
</thead>
<tbody>
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<tr>
<td>F</td>
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<td>376</td>
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<tr>
<td>G</td>
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<tr>
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<td>U</td>
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<tr>
<td>X</td>
<td>342</td>
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</tr>
</tbody>
</table>

Mean       | 391  | 402  | 12     |
8.5 Change in QTc Interval Using the Fridericia Method

The Fridericia method is the second of two methods for calculating QTc required by the FDA when a pharmaceutical company submits data about drug effects on QT interval. This method is more accurate for estimating QT interval for heart rates above 60 beats per minute. It is included for comparison consistency with the FDA data requirements.
### Table 4

*Change in QTc interval using Fridericia Method (ms)*

<table>
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<th>Change</th>
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<td>D</td>
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<tr>
<td>Mean</td>
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<td>394</td>
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</table>
Figure 5. Individual subjects’ change in QTc interval using Fridericia method (units = ms). Green dotted line represents decrease heart rate subjects (Pre > Post). Red solid line represents increase heart rate subjects (Pre < Post).

8.6 Change in QTc Interval Using the Framingham Method

The Framingham method for calculating QTc is a linear function of the RR interval. One published investigation comparing four different methods for calculating QTc interval found the Framingham method more accurate than the Bazett, Fridericia, and Hodges methods for heart rates over 60 beats per minute. These data are included for providing best estimates and overall greater data analysis precision.
### Change in QT interval using Framingham Method (ms)

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Pre</th>
<th>Post</th>
<th>Change</th>
</tr>
</thead>
<tbody>
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<tr>
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<td>423</td>
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<td>C</td>
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<td>436</td>
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<tr>
<td>D</td>
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<tr>
<td><strong>Mean</strong></td>
<td>384</td>
<td>393</td>
<td><strong>9</strong></td>
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</table>
8.7 Change in QTc interval Using the Rubal (a novel linear regression) Method

The Bazett and Fridericia methods for QT correction were proposed in 1920. The Framingham method was proposed in 1992 to reduce the QTc estimation errors associated with prior methods. Luo et al. (2004) point out that none of these methods fully removes the influence of heart rate from estimating QT interval.\(^5\)

For the present data, the relationship between QT and RR interval (inverse of heart rate) is illustrated in Figure 8. A strong correlation \(r = 0.87, p < 0.001\) can be seen between QT and RR interval for the unadjusted subject EKGs. Correcting QT interval as a function of RR interval variability eliminates the correlation \(r = 0.8E^{-6}, p = 0.999\) between QTc and RR interval, as shown in Figure 8. Appendix D provides greater detail about the Rubal method for QTc adjustment.
Figure 7. QT interval unadjusted for RR interval.

Figure 8. QT interval after linear regression adjustment for RR interval.
Table 6

*Change in QTc interval using Rubal Method (ms)*

<table>
<thead>
<tr>
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<th>Change</th>
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<tr>
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<td>408</td>
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<tr>
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<td>414</td>
<td>432</td>
<td>17</td>
</tr>
</tbody>
</table>
Figure 9. Individual subjects’ QTc change using Rubal method (units = ms). Green dotted line represents decrease heart rate subjects (Pre > Post). Red solid line represents increase heart rate subjects (Pre < Post).

8.8 Summary QT interval Change

A t-test of Pre- and Post-QT intervals for all subjects shows a significant lengthening of the QTc interval using the Rubal method ($p = 0.03$), non-significant difference using the Bazett and Framingham methods, and a trend using the Fridericia method ($p = 0.6$). The magnitude of the change for any method does not reach the 30 ms clinical significance threshold.
Table 7

*Comparison of Mean QT interval Change Calculation Methods*

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<th>M</th>
<th>t</th>
<th>p</th>
<th>r</th>
</tr>
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<td>0.16</td>
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<tr>
<td>Post</td>
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<td></td>
</tr>
<tr>
<td>Fridericia</td>
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</tr>
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<td>0.06</td>
<td>0.38</td>
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<tr>
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<td></td>
<td></td>
</tr>
<tr>
<td>Framingham</td>
<td></td>
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<td></td>
</tr>
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<td>0.18</td>
<td>0.28</td>
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</table>

*Note.* M = mean; t = t-test statistic; p = p-value; r = correlation (effect size).

Table 8

*Magnitude of QTc Exceeding Thresholds*

<table>
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<th>450 ms</th>
<th>480 ms</th>
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<td>Pre 1</td>
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</tr>
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<td>Pre 0</td>
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<td>Pre 0</td>
</tr>
<tr>
<td>Rubal</td>
<td>Pre 5</td>
<td>Post 7</td>
<td>Pre 5</td>
</tr>
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</table>

*Note.* N = 24

8.9 QT Lengthening Versus QT Shortening Analysis

In Sections 8.2 and 8.7, the mean changes in heart rate and QTc interval, respectively, do not show any clinically significant difference. Visual inspection of the pre- and post-exposure results suggest that the subjects are divided into two groups, those with an increase in heart rate and/or QTc interval and those with a decrease in heart rate and/or QTc interval. Increased QTc interval carries a risk of future adverse cardiac events. It is possible that two subpopulations have opposite responses to HEMI exposure, with the...
opposing effects canceling any mean effect. Examining the subpopulations was undertaken to determine if an increase in QTc interval was present using threshold values of 40 ms from clinical care guidelines (Drew et al. 2010), plus 30 ms and 60 ms from the FDA Guidelines for Industry (US Dept. HHS). Analyzing the pre- and post-exposure data using the four methods of QTc calculation showed the following QTc differences.

### Table 9

<table>
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<th>QTc Shortening</th>
<th>QTc Lengthening</th>
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</thead>
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<tr>
<td>Post</td>
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</tr>
<tr>
<td>Post</td>
<td>408</td>
<td></td>
</tr>
</tbody>
</table>

*Note.* M = mean; t = t-test statistic; r = correlation (effect size).

* *p < 0.05, **p < 0.01, ***p < 0.001.

EKGs showed significant change in mean QTc interval with each of the four methods for QTc calculation found within both the QTc shortening and QTc lengthening sub-groups.

QTc shortening has been suggested as a risk for adverse cardiac events. In one study a lower QTc interval of ≤ 377 ms was associated with a hazard ratio of 1.36 for cardiovascular disease mortality. The Bazett, Fridericia, and Framingham methods for calculating QTc interval all identify eight or nine subjects with a pre-exposure QTc ≤ 377 ms and six or seven subjects with a post-exposure QTc ≤ 377 ms. The Rubal method identifies four subjects with a pre-exposure QTc ≤ 377 ms and no subject with a post-exposure QTc ≤ 377 ms. Using the Rubal method, the four subjects showed post-exposure QTc lengthening above 377 ms and none of the other subjects showed QTc shortening to ≤ 377 ms. These results suggest the Rubal method is superior when
evaluating an EKG for QTc shortening. Because this study was not designed to examine QTc shortening, it will not be discussed further.

Using the Bazett and Framingham methods, 13 of 24 subjects had a statistically significant lengthening of the QTc interval. The Fridericia method showed 15 of 24 subjects with a statistically significant longer QTc interval. The Rubal method showed 17 of 24 subjects with a QTc statistically significant lengthening. Examining the mean for subjects with QTc lengthening, the Framingham, Rubal, and Bazett methods all showed a change greater than 30 ms, the FDA defined borderline threshold. The Bazett method also showed QTc lengthening just shy of the alert levels of 40 ms clinically significant threshold. Examining individual responses using the four QTc calculation methods showed the FDA threshold for prolonged QTc change of 60 ms was exceeded by two subjects using the Bazett, Fridericia, and Framingham methods. The Rubal method showed three subjects with a QTc interval exceeding 60 ms and a fourth subject at 59 ms.

Table 10

<table>
<thead>
<tr>
<th>QTc</th>
<th># Exceeding 30 ms</th>
<th># Exceeding 40 ms</th>
<th># Exceeding 60 ms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bazett</td>
<td>5/13</td>
<td>5/13</td>
<td>2/13</td>
</tr>
<tr>
<td>Fridericia</td>
<td>5/15</td>
<td>4/15</td>
<td>2/15</td>
</tr>
<tr>
<td>Framingham</td>
<td>5/13</td>
<td>5/13</td>
<td>2/13</td>
</tr>
<tr>
<td>Rubal</td>
<td>6/17</td>
<td>4/17</td>
<td>3/17</td>
</tr>
</tbody>
</table>

One subject exceeded the 500 ms threshold post-exposure for all four methods, considered a significant risk for adverse cardiac events. This subject also exceeded the threshold for a prolonged QTc interval before HEMI exposure using the Bazett and Rubal methods, suggestive of an underlying long QT syndrome. Identification of this individual was not possible before HEMI exposure. This subject’s results reveal nothing about the general population prevalence of QTc exceeding 500 ms after a 5-second HEMI exposure. Tables 11 through 14 show the results of repeating the analyses after removing this subject. The Rubal linear regression was recalculated using $N = 23$, so the resulting calculations yielded slightly different results.
Table 11

*Comparison of Mean QT interval Change Calculation Methods (N = 23)*

<table>
<thead>
<tr>
<th>QTc</th>
<th>M</th>
<th>t</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Bazett</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>388</td>
<td>1.11</td>
<td>0.28</td>
<td>0.23</td>
</tr>
<tr>
<td>Post</td>
<td>396</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fridericia</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Pre</td>
<td>380</td>
<td>1.66</td>
<td>0.11</td>
<td>0.33</td>
</tr>
<tr>
<td>Post</td>
<td>389</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Framingham</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Pre</td>
<td>381</td>
<td>1.03</td>
<td>0.31</td>
<td>0.21</td>
</tr>
<tr>
<td>Post</td>
<td>388</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rubal</td>
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<tr>
<td>Pre</td>
<td>410</td>
<td>1.88</td>
<td>0.07</td>
<td>0.37</td>
</tr>
<tr>
<td>Post</td>
<td>424</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

*Note.* M = mean; t = t-test statistic; p = p-value; r = correlation (effect size).

A t-test of Pre- and Post-QT interval for all subjects no longer shows a significant lengthening of the QTc interval using any of the four methods, though a trend is seen using the Rubal method (p = .07). The magnitude of the change for any method does not reach the 30 ms clinical significance threshold.

Table 12

*Magnitude of QTc Exceeding Thresholds (N = 23)*

<table>
<thead>
<tr>
<th>QTc</th>
<th>440 ms</th>
<th>450 ms</th>
<th>480 ms</th>
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<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
</tr>
<tr>
<td>Bazett</td>
<td>0</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Fridericia</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Framingham</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Rubal</td>
<td>4</td>
<td>6</td>
<td>4</td>
</tr>
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</table>
Table 13

*QTc Shortening versus QTc Lengthening (N = 23)*

<table>
<thead>
<tr>
<th>QTc</th>
<th>M</th>
<th>n</th>
<th>t</th>
<th>r</th>
<th>M</th>
<th>n</th>
<th>t</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bazett</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>396</td>
<td>11</td>
<td>-5.83***</td>
<td>0.88</td>
<td>381</td>
<td>12</td>
<td>4.04**</td>
<td>0.77</td>
</tr>
<tr>
<td>Post</td>
<td>375</td>
<td></td>
<td></td>
<td></td>
<td>416</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fridericia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>384</td>
<td>9</td>
<td>-5.38***</td>
<td>0.88</td>
<td>377</td>
<td>14</td>
<td>3.45**</td>
<td>0.69</td>
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<tr>
<td>Post</td>
<td>371</td>
<td></td>
<td></td>
<td></td>
<td>401</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Framingham</td>
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<td></td>
</tr>
<tr>
<td>Pre</td>
<td>390</td>
<td>11</td>
<td>-4.86***</td>
<td>0.84</td>
<td>374</td>
<td>12</td>
<td>4.04**</td>
<td>0.77</td>
</tr>
<tr>
<td>Post</td>
<td>372</td>
<td></td>
<td></td>
<td></td>
<td>402</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rubal</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>427</td>
<td>8</td>
<td>-3.87**</td>
<td>0.83</td>
<td>401</td>
<td>15</td>
<td>3.45**</td>
<td>0.68</td>
</tr>
<tr>
<td>Post</td>
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<td></td>
<td></td>
<td></td>
<td>430</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note.* M = mean; t = t-test statistic; r = correlation (effect size).

* p < 0.05, ** p < 0.01, *** p < 0.001.

EKGs still showed significant difference in mean pre- versus post-exposure QTc interval with each of the four methods for QTc calculation for the QTc lengthening sub-group.

Using the Bazett and Framingham methods, 12 of 23 subjects had a statistically significant lengthening of the QTc interval. The Fridericia method showed 14 of 23 subjects with a statistically significant longer QTc interval. The Rubal method showed 15 of 23 subjects with a QTc statistically significant lengthening. Examining the mean for subjects with QTc lengthening, only the Bazett method showed a change greater than 30 ms, the FDA defined borderline threshold. The Fridericia, Framingham, and Rubal methods showed mean changes of 24, 28, and 29 ms, respectively. Examining individual responses using the four QTc calculation methods showed the FDA threshold for prolonged QTc change of 60 ms was exceeded by one subject using the Bazett, Fridericia, and Framingham methods. The Rubal method showed two subjects with a QTc interval exceeding 60 ms and a third subject at 59 ms.
Table 14

*QTc Lengthening Exceeding Thresholds (N = 23)*

<table>
<thead>
<tr>
<th>Method</th>
<th># Exceeding 30 ms</th>
<th># Exceeding 40 ms</th>
<th># Exceeding 60 ms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bazett</td>
<td>4/12</td>
<td>4/12</td>
<td>1/12</td>
</tr>
<tr>
<td>Fridericia</td>
<td>4/14</td>
<td>3/14</td>
<td>1/14</td>
</tr>
<tr>
<td>Framingham</td>
<td>4/12</td>
<td>4/12</td>
<td>1/12</td>
</tr>
<tr>
<td>Rubal</td>
<td>4/15</td>
<td>3/15</td>
<td>2/15</td>
</tr>
</tbody>
</table>

9.0 **DISCUSSION**

The results of this study show that lengthening of the QT interval can occur after a single 5-second HEMI exposure. Several methods exist for correcting the QT interval to remove the influence of heart rate, or inverse of RR interval. Refer to Table 7 for a summary comparison of mean QTc interval changes. The Bazett, Fridericia, and Framingham methods are recognized as useful by the FDA when assessing the impact of a pharmaceutical on QTc interval. The Bazett method is most widely used, but this method over-estimates QT interval for heart rates above 60 beats per minute. The Fridericia and Framingham methods for correcting QT interval are less influenced by heart rate, but still have significant unaccounted variability. The Rubal method accounts for almost all variability of QTc interval through a linear regression.

Two population subsets appear to be present, those who respond to HEMI exposure with QTc lengthening and those who respond with QTc shortening. The QTc lengthening and shortening both reach statistical significance. A smaller subset of subjects show a mean QTc lengthening that exceeds one or more thresholds for risk of adverse cardiac events. One subject appears to be an outlier, with a baseline QTc interval exceeding 450 ms for both the Bazett and Rubal methods, and post-exposure QTc interval exceeding 500 ms for all four methods. It is possible that this individual has an underlying congenital QT prolongation, as previously noted to have prevalence estimates from 1/20,000 to 1/2,500.6 After removing this subject’s data, mean QTc lengthening and shortening are still statistically significant for all four QTc correction methods. The mean QTc lengthening exceeds QTc variability of 16 ms for all four methods.

The clinical or operational significance of QTc interval change can be assessed by absolute magnitude or relative change in QTc interval. In practice a common clinical threshold for QTc interval with an increased risk of adverse cardiac events is ≥ 440 ms.20,21,22 These three studies calculated the risk of adverse cardiac events using the Bazett method. In comparison the FDA uses 450 ms and 480 ms thresholds for identifying the risk of adverse cardiac events. Both the Bazett and Fridericia methods for correcting QTc interval are requested by the FDA, plus acceptance of the Framingham method if the submitter chooses to provide additional results. After HEMI exposure, using the Bazett method and n = 23, four subjects have a QTc interval greater than 440 ms.
ms and two subjects exceed 450 ms. The Fridericia and Framingham methods do not identify any subject as exceeding the 440 ms threshold. The Rubal method identifies four subjects exceeding 440 ms before HEMI exposure, six exceeding 440 ms after exposure, three subjects exceeding 450 ms before exposure and six subjects exceeding this threshold after exposure. Except for the one outlier removed from this discussion, no subject exceeded 480 ms before or after HEMI exposure using any of the four QTc calculation methods. The subjects in the current study represent a healthier population from the populations in the three studies that identified a risk when QTc exceeds 440 ms. None of the subjects in the current study have a history of heart disease and all engage in regular aerobic exercise as part of military fitness training. These differences likely place the subjects with QTc intervals exceeding 440 ms after HEMI exposure at borderline risk for adverse cardiac events.

The FDA also specifies change in QTc interval of 30 ms as borderline and 60 ms as significant for risk of an adverse cardiac event. A 40 ms increase in QTc interval was chosen as a threshold level for the current study prior to knowledge of the FDA thresholds. In the current study, with the outlier removed, one third of subjects exceed a 40 ms change in QTc interval, using the Bazett and Framingham methods. Approximately one fifth of subjects exceed a 40 ms QTc change using the Fridericia and Rubal methods. One subject exceeds a 60 ms QTc change by all four methods. These results indicate that a sizable minority of subjects develop a borderline or significant change in QTc interval after a single 5-second HEMI exposure.

It is possible that the combination of medication(s) and electrical shock, both reported to lengthen the QT interval, results in clinically defined QT prolongation not seen with either exposure alone. One review of HEMI safety for law enforcement noted over 70% of individuals subdued using HEMI had intoxicating drugs in the urine. Cocaine was the most common substance detected at 40% for individuals who were screened. A detailed list of medications that can cause QT prolongation can be found at www.Crediblemeds.org. Exploring drug-HEMI interactions was beyond this current investigation, but should be considered as part of the critical assessment for HEMI exposure under operational conditions. Certainly adding combinations of common pharmaceutical and/or abuse drug use should be a basis for future HEMI effects research.

The cardiac action potential is shown below in Figure 2. The QT interval consists of phases 0 through 3. Opening of the potassium channels during phase 3 repolarizes or returns the membrane potential toward the resting state. Blocking the potassium repolarizing current channel (IKr) prevents the outflow of potassium from cardiac myocytes, prolonging the QT interval. It is possible that HEMI can result in dysfunction of the IKr channels. Why some people but not others experience this effect is unclear. It is possible that genetic variation of the proteins comprising the IKr channels predisposes people to the development of QTc lengthening after HEMI exposure.
Another important question not addressed in this study is: Do multiple HEMI exposures have a greater influence on QT prolongation? No investigations have been found in the literature. Concerning longer HEMI exposures, two published studies have evaluated the effects of extended duration HEMI exposures. Dawes et al. studied 11 volunteers exposed for 30 seconds to HEMI from a TASER C2 device. Before and after exposure EKGs were evaluated by a cardiac electrophysiologist who was blind to the identity of the subjects. Result descriptions were limited to rate, rhythm, and possible ST depression. No comment was provided about QT interval. A second study by Dawes et al. exposed 53 volunteers to a TASER X3 device for 10 seconds. No EKG results were reported. Does this change for an individual with HEMI exposures on different days?

These questions and others should be considered for future research, especially a study QT lengthening after extended duration HEMI exposures.
10.0 CONCLUSIONS

Twenty-four healthy volunteers were investigated using EKG after receiving a 5-second HEMI exposure as part of USAF Security Forces training. Standard 12-lead EKGs were obtained before exposure and less than 30 minutes after the single 5-second exposure. All EKGs were analyzed for RR and QT intervals. The QT interval was corrected for RR variability by four methods, Bazett, Fridericia, Framingham, and Rubal, a novel linear regression method. Two subpopulations were identified, those who developed QTc shortening and those who developed QTc lengthening. Both subpopulations had statistically significant changes in QTc interval. One third of one subpopulation were found to exceed the FDA threshold for borderline QTc lengthening. A single individual with existing pre-exposure QTc prolongation exceeded a 500 ms threshold for significant risk of adverse cardiac events.
REFERENCES


APPENDIX A – Medical Screening Form

Subject ID #: ______________________

Part I - Directions:
These questions are being asked to ensure your safety in this study

Circle YES – If any of the below medical conditions or medications apply to you.

Circle NO – If ALL of the listed medical conditions and medications do NOT apply to you.

Circle UNSURE – If you do not know about any of the listed medical conditions or medications.

Do Not Circle any Individual Medical Condition or Medication.

1. Do you have a medical waiver for continued military service? YES NO UNSURE

2. Do you currently take any of the following medications? YES NO UNSURE

Congestive heart failure
Abnormal heart rhythm, fast or slow
Irregular heartbeats that make you short of breath or lightheaded
Recurrent chest pains
Angina with mild to moderate exercise
Heart attack
Cardiac pacemaker
Implanted cardioverter-defibrillator (AICD)
Irritated heart muscle (Cardiomyopathy)
Delay in heartbeat conduction (heart block)

2. Do you currently take any of the following medications? YES NO UNSURE

Antiarrhythmic drugs
Amiodarone (Cordarone)
Bretylium (Bretylol)
Disopyramide (Norpace)
Dofetilide (Tikosyn)
Flecainide (Tambocor)
Ibutilide (Corvert)
Procainamide (Pronestyl, Procan)
Quinidine (Quinidex, Quinaglute)
Sotalol (Betapace)

(over)
Do you currently take any of the following medications? (cont.)

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<th>Psychiatric drugs</th>
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<th>NO</th>
<th>UNSURE</th>
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<td>Amitriptyline (Elavil)</td>
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<td></td>
<td></td>
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<tr>
<td>Chlorpromazine (Thorazine)</td>
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<td></td>
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<tr>
<td>Clomipramine (Anafranil)</td>
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<tr>
<td>Desipramine (Norpramin)</td>
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<td>Doxepin (Adapin)</td>
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<td>Ziprasidone (Geodon, Zeldox)</td>
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<td>Fluconazole (Diflucan)</td>
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<td>Pentavalent antimonial meglumine (Glucantime)</td>
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<td>Diphenhydramine (Benadryl)</td>
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<td>Hydroxyzine (Atarax)</td>
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<td>Loratidine (Claritin)</td>
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<th>Miscellaneous</th>
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<td>Cocaine</td>
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<td>Organophosphates (pesticides)</td>
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<td>Papaverine</td>
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<td>Tacrolimus (Prograf)</td>
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APPENDIX B - Selvester QRS Screening Criteria

The Selvester QRS screening criteria were used to identify Q-wave infarction.

(1) Q wave of $\geq 30$ ms in aVF (inferior);
(2) Q wave of $\geq 40$ ms in I and aVL (lateral);
(3) Q wave of $\geq 40$ ms in $\geq$ two of V4 through V6 (apical);
(4) R wave of $\geq 40$ ms in V1 (posterior); (5) any Q wave in V2 (anterior); and
(5) R wave $\leq 0.1$ mV and 10 ms in lead V2 (anterior).
### APPENDIX C - Cardiac Medical Conditions Disqualifying for Military Service

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<tr>
<th>Disqualifying for continued military service</th>
<th>Comments</th>
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<tr>
<td>Congestive heart failure</td>
<td>Heart inadequately pumps blood, poor exercise tolerance</td>
</tr>
<tr>
<td>Persistent major rhythm disturbances</td>
<td>At risk for sudden cardiac death</td>
</tr>
<tr>
<td>Repeated angina attacks</td>
<td>Chest pain = warning sign of potential heart attack</td>
</tr>
<tr>
<td>Silent ischemia at low to moderate workload</td>
<td>Can only be diagnosed with exercise test</td>
</tr>
<tr>
<td>Evidence of myocardial infarction</td>
<td>Found on EKG when otherwise asymptomatic (silent heart attack)</td>
</tr>
<tr>
<td>Medication for treatment or prevention of:</td>
<td>Some of the same medications are used to manage high blood pressure, migraines, and other medical conditions</td>
</tr>
<tr>
<td>Angina</td>
<td>identified at risk for sudden death</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>satisfactory performance is the key</td>
</tr>
<tr>
<td>Major rhythm disturbance</td>
<td>At risk for sudden death</td>
</tr>
<tr>
<td>(ventricular tachycardia, ventricular fibrillation, symptomatic paroxysmal supraventricular tachycardia, atrial flutter, or atrial fibrillation)</td>
<td></td>
</tr>
<tr>
<td>Pacemaker or implanted cardioverter</td>
<td></td>
</tr>
<tr>
<td>defibrillator</td>
<td></td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td></td>
</tr>
<tr>
<td>Symptomatic premature ventricular contractions that interfere with satisfactory performance of duty</td>
<td></td>
</tr>
<tr>
<td>Second degree Type II or third degree heart block</td>
<td></td>
</tr>
<tr>
<td>Symptomatic second degree Type I heart block</td>
<td></td>
</tr>
</tbody>
</table>

Distribution A. Distribution authorized for public release.
APPENDIX D - Rubal Method for Correcting QT Interval Based on RR Interval

Rubal scores are constructed from RR Interval (sec) and QT (ms) scores (see Table 15 below). Using these values, we calculated: QT/RR, average of all 48 QT/RR measurements (mean = \( \bar{y} = 423.13 \)), and predicted QT/RR from a regression analysis using RR interval (sec) as an independent variable (see Figure 11 below, top figure). This analysis yielded a regression line equation for predicted QT/RR scores (\( y = -369.55x + 758.81 \)) and was used to calculate the predicted QT/RR scores for each subject. A strong correlation between RR interval and QT interval can be seen, with \( R^2 = 0.76 \). The influence of RR interval on QT interval was significantly reduced using the following equation.

\[
\text{QTc (Rubal)} = y - y' + \bar{y}
\]

- \( y \) = measured QT/RR
- \( y' \) = Predicted of QT/RR
- \( \bar{y} \) = Average of all QT/RR

We named these new values Rubal, because Bernard Rubal, Ph.D., our physiologist collaborator, suggested this method to strongly reduce the influence RR intervals have on QT intervals. To demonstrate the variability associated with RR intervals was significantly reduced, we ran a regression predicting Rubal scores using RR intervals as an independent variable. As expected, RR interval scores did not influence Rubal scores, as indicated by a low \( r \) (see Figure 11, bottom figure). Furthermore, QTc (Rubal) is currently the only method that is not contaminated by RR intervals: Bazett, Fridericia, and Framingham are highly correlated with RR intervals (see Table 16).
Table 15

Raw scores for RR Interval (sec), QT Interval (ms), QT/RR, Predicted QT/RR, and QTc (Rubal)

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>RR Interval (sec)</th>
<th>QT (ms)</th>
<th>QT/RR</th>
<th>Predicted QT/RR</th>
<th>QTc (Rubal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1.02</td>
<td>0.88</td>
<td>393</td>
<td>360</td>
<td>387</td>
</tr>
<tr>
<td>B</td>
<td>0.70</td>
<td>0.77</td>
<td>353</td>
<td>387</td>
<td>507</td>
</tr>
<tr>
<td>C</td>
<td>0.95</td>
<td>0.79</td>
<td>417</td>
<td>403</td>
<td>439</td>
</tr>
<tr>
<td>D</td>
<td>0.88</td>
<td>0.97</td>
<td>387</td>
<td>400</td>
<td>439</td>
</tr>
<tr>
<td>E</td>
<td>0.71</td>
<td>0.81</td>
<td>343</td>
<td>360</td>
<td>484</td>
</tr>
<tr>
<td>F</td>
<td>0.89</td>
<td>1.03</td>
<td>340</td>
<td>380</td>
<td>383</td>
</tr>
<tr>
<td>G</td>
<td>0.88</td>
<td>1.16</td>
<td>367</td>
<td>380</td>
<td>417</td>
</tr>
<tr>
<td>H</td>
<td>0.84</td>
<td>0.79</td>
<td>370</td>
<td>367</td>
<td>439</td>
</tr>
<tr>
<td>I</td>
<td>0.73</td>
<td>0.78</td>
<td>373</td>
<td>367</td>
<td>514</td>
</tr>
<tr>
<td>J</td>
<td>0.78</td>
<td>0.91</td>
<td>370</td>
<td>370</td>
<td>472</td>
</tr>
<tr>
<td>K</td>
<td>0.73</td>
<td>0.65</td>
<td>357</td>
<td>340</td>
<td>486</td>
</tr>
<tr>
<td>L</td>
<td>0.76</td>
<td>0.66</td>
<td>320</td>
<td>343</td>
<td>419</td>
</tr>
<tr>
<td>M</td>
<td>0.85</td>
<td>0.96</td>
<td>360</td>
<td>373</td>
<td>422</td>
</tr>
<tr>
<td>N</td>
<td>1.32</td>
<td>1.07</td>
<td>413</td>
<td>400</td>
<td>314</td>
</tr>
<tr>
<td>O</td>
<td>1.07</td>
<td>0.97</td>
<td>353</td>
<td>360</td>
<td>331</td>
</tr>
<tr>
<td>P</td>
<td>1.01</td>
<td>0.82</td>
<td>377</td>
<td>360</td>
<td>374</td>
</tr>
<tr>
<td>Q</td>
<td>1.11</td>
<td>1.38</td>
<td>390</td>
<td>393</td>
<td>351</td>
</tr>
<tr>
<td>R</td>
<td>0.86</td>
<td>0.88</td>
<td>360</td>
<td>413</td>
<td>419</td>
</tr>
<tr>
<td>S</td>
<td>0.81</td>
<td>0.88</td>
<td>353</td>
<td>343</td>
<td>434</td>
</tr>
<tr>
<td>T</td>
<td>0.96</td>
<td>1.21</td>
<td>337</td>
<td>347</td>
<td>351</td>
</tr>
<tr>
<td>U</td>
<td>0.80</td>
<td>0.75</td>
<td>403</td>
<td>467</td>
<td>506</td>
</tr>
<tr>
<td>V</td>
<td>1.08</td>
<td>1.17</td>
<td>420</td>
<td>417</td>
<td>388</td>
</tr>
<tr>
<td>W</td>
<td>1.09</td>
<td>0.96</td>
<td>377</td>
<td>400</td>
<td>346</td>
</tr>
<tr>
<td>X</td>
<td>0.84</td>
<td>0.68</td>
<td>313</td>
<td>377</td>
<td>373</td>
</tr>
</tbody>
</table>
Figure 11. QT/RR and Rubal Method

![Graph showing the relationship between QT/RR and RR interval for the Rubal method.](image)

\[ y = -0.0017x + 423.13 \]
\[ r^2 = 7E-11, \, p = .999 \]

Table 16

Correlations (r) between QTc and RR interval

<table>
<thead>
<tr>
<th>RR Interval</th>
<th>Bazett</th>
<th>Framingham</th>
<th>Fridericia</th>
<th>Rubal</th>
</tr>
</thead>
<tbody>
<tr>
<td>QTc</td>
<td>-0.64***</td>
<td>-0.52***</td>
<td>-0.38**</td>
<td>-0.8E-3***</td>
</tr>
</tbody>
</table>

*p < 0.05, **p < 0.01, ***p < 0.001.