University of New Hampshire

FEAIRHELLER 2020 PROJECT OUTLINE: IRB #8242

INTRODUCTION

Global hypertension rates have reached epidemic proportions with upwards of one billion individuals diagnosed and estimates that 1/3 of the global adult population is hypertensive.[1] Blood pressure (BP) is a primary risk factor for cardiovascular disease.[2,3] There are over a million firefighters in America, and firefighting is one of the most hazardous and dangerous jobs with an inherent increased risk of death, just by nature of the work. In fact, many firefighters have hypertension, and cardiac-related incidents are the leading cause of death among firefighters.[4,5,6] Also, BP control remains an issue in firefighters, with close to 74% of hypertensive firefighters not having adequate control of their BP.[7] Research that examines BP in firefighters is scarce, and quantifying the BP surge that occurs with pager activation has never been done.

It is known that exercise training improves cardiovascular health, lowers lipid levels, reduces inflammation, and reduces BP. Yet, it is interesting that the National Fire Protection Agency (NFPA) does not require fire companies to have fitness testing or programing for the crew. The NFPA has established that the demands of firefighting require a fitness level of a VO_{2max} equivalent of 42 ml/kg/min.[8] Yet, only 20% of volunteer firefighters meet this fitness threshold.[9] And, even worse is that <30% of fire stations have a fitness program or fitness monitoring as part of their standard operating procedures.

It is also known that a healthy diet improves cardiovascular health, lowers lipid levels, reduces inflammation, and reduces BP. Evidence suggests that the Mediterranean diet can improve cardiovascular health, and the Mediterranean diet has been touted the top heart-healthy diet for 2 years in a row.[10] The diet includes a high consumption of fruits and vegetables, a moderate consumption of fish, nuts, low-fat diary, and wine, and a low consumption of red meat and other meat products. Dietary patterns like this reduce inflammation and improve vascular function, which will benefit firefighters. Firefighters know that diet is important, yet they don't know how to modify their diet. Importantly, a recent survey study done at Harvard found that the Mediterranean diet is one that firefighters actually would prefer.[11]

It is not known whether an exercise and diet intervention can reduce the blood pressure surge that occurs when a pager alarm sounds. ABP monitoring is an at home BP monitoring system, which has recently been clinically recommended by guidelines. Normal morning BP surge is established as a physiological event, yet an exaggerated surge is a known cardiovascular risk.[12] Therefore it can be assumed that the BP surge that occurs with pager alarms must also present severe risk. In prior studies, we have found that the BP surge with pager alarm in firefighters can be extreme.

SPECIFIC AIMS

This intervention study seeks to measure the BP surge with pager alarm and examine whether a 6-week intervention (self-report exercise training and Mediterranean diet) leads to changes in the BP surge.

The purpose of our study is to:

(1) compare data between two intervention groups (firefighters and civilians) to determine whether an exercise and diet intervention influences the magnitude of BP surge that occurs with pager alarms.

(2) compare data between two intervention groups (firefighters and civilians) to determine whether an exercise and diet intervention reduces cardiovascular risk* and improves fitness levels.

(3) cross-sectional examination of data within the groups to evaluate relationships between the magnitude of BP surge that occurs with pager alarms and cardiovascular risk*. This is an important preliminary step to determine what could be related to the BP surge and will drive future research.

*We will assess cardiovascular risk by clinical BP, body composition through bioelectrical impedance, lipid levels through finger stiffness, vascular stiffness by pulse wave velocity, inflammation and oxidative stress levels by serum analysis from blood draws.

RESEARCH PROTOCOL

This study is a pre-post exercise and diet intervention study with 2 groups: firefighters and civilians. For the study, firefighters will be recruited from local fire departments and civilians will be recruited from the surrounding areas. The only compensation will be for parking while they are on campus for testing appointments. A study description document is attached which will be used to supplement the word-of-mouth advertising done by walking into local firehouses.

The population is seemingly healthy and low-risk, so physician referral or approval is not needed. Criteria for inclusion: adult 18 years of age and older; no history of renal disease, diabetes, or cardiovascular incident requiring surgery; no existing orthopedic issues that preclude exercise; no more than one anti-hypertensive or cholesterol medication.

Brief protocol summary:

Study participants from both groups (firefighters & civilians) will be enrolled for a total of about 8 weeks. During this time period they will complete the following steps:

1. Orientation and informed consent (15-30 min)

   Each participant will provide informed consent and complete a health/exercise history questionnaire. Consent will be obtained in a face-to-face meeting by the principle investigator, Deborah Feairheller. The study will be explained, any questions answered, and then consent will be signed. Each participant will receive a copy of the signed consent form.

2. Diet training (includes a study manual and a 45-minute training session with study personnel)

   Dietary training will be provided. This will include the study manual (attached to application email) and a 45-minute session where the study participants are taught about the Mediterranean diet and given specific instructions on serving sizes for the food groups.

3. Pre-intervention testing
   a. Morning fasted study (45 min)
   b. Fitness test session (45 min)
   c. Blood pressure monitoring (includes wearing an ambulatory blood pressure monitor for 12-hours and a 30 min appointment to get set-up on the monitor)

4. At-home and self-report 6-week intervention (circuit workout 3-times per week and a Mediterranean diet)

   Each participant will undergo 6-weeks of intervention (diet and exercise). They will self-report the number of times per week that they complete the circuit workout, and they will self-report the number of servings per food group that they eat while following the diet. The workouts are done at home, in the fire station, or in a fitness center.

5. Post-intervention health and fitness testing which will be the same as pre-testing (#3).

The specifics of each of the appointments are outlined below. During each visit to the lab, to confirm and remind what the study includes, each participant will receive a verbal explanation of the measures collected that day and asked if they have any questions. They will also be asked if they still provide consent.

Orientation & Consent

Study participants will learn about the study, have questions answered and review the consent form. They will complete the wellness questionnaire.

They will also complete a short 21-item scale that asks questions related to their feelings over the past week. One of the main components of blood pressure is emotional response, so for this study we will also assess participants stress and anxiety levels with the Depression, Anxiety, and Stress Scales (DASS-21) scale. The DASS-21 is a 21-item self-reported scale that will determine the presence and severity of the three listed psychometric characteristics above.

The reliabilities of the DASS-21 (internal consistencies) Anxiety, Depression, Stress, and Total scales are 0.88 (95% CI = 0.87–.89) for the Depression scale, 0.82 (95% CI = 0.80–.83) for the Anxiety scale, 0.90 (95% CI = 0.89–.91) for the Stress scale, and 0.93 (95% CI = 0.93–.94) for the Total scale.

The DASS-21 may be administered and scored by non-psychologists, and none of the items refers to suicidal tendencies. The primary function of the DASS-21 is to assess the severity of symptoms of depression, anxiety and stress. Since the scale was developed with non-clinical samples, it is suitable for even adolescents and adults, so can be considered low risk. Despite it being low risk, a comment has been placed in the Risk section of the consent form that states: "The risk associated with completing this short 21-item survey is that you may feel uncomfortable while answering the questions. If you feel this and your symptoms are severe, we will work with you to refer you to a proper clinician who is part of your health network."

Pre-Intervention Testing Visits

All participants will complete three testing components during pre-intervention. This includes a morning ***fasted study***, a ***blood pressure monitoring***, and a ***fitness test***. We coordinate these appointment times to fit into participant's schedule.

Fasted Testing Appointment*:*

The total time for this visit will be around 45 minutes. This test will occur on UNH campus in NH Hall. They will be required to fast for 10 hours before coming into the lab for the testing. For this visit, we ask that they avoid food or drink (water is allowed) for at least 10 hours before coming into the lab. We also ask that they avoid alcohol and exercise the night before. Height, weight, and blood pressure will be taken. Body composition will be measured, glucose and cholesterol levels measured, a blood draw collected, and blood vessel ultrasound and pressure studies will be done.

Considering that the population is seemingly healthy based on other exclusion criteria, it is still possible to identify high blood pressure or high lipid/glucose levels in the participants. This would not be an exclusion from the study. If this occurs, we inform them and offer to provide them with the data, if they wanted to follow-up with their physician.

Body composition test will tell the investigators what percentage of the body is fat, muscle and bone. The instrument that measures body composition is called bioelectrical impedance (BIA). The machine will cause a very small current to travel through the body for 2-3 seconds, but nothing will be felt. To do this test, they will lie on a table on their back with left foot exposed. To collect the measurements, a technician will place two electrodes on the left foot and two electrodes on left hand.

Blood glucose and cholesterol measurements will tell the investigators what the levels of fasted plasma glucose and cholesterol are. We will be measuring these with a finger-prick test. Only one finger prick will occur, and a single large drop of blood will be collected.

Plasma inflammation, oxidative stress, and vasodilation levels. A blood draw will occur where we collect 2 tubes of blood (equivalent of 7 tsp or 1.2 oz). This will allow us to measure common markers that circulate in the blood which are related to heart health.

Blood vessel ultrasound and pressure measures. We will be checking the function of blood vessels through the use of several machines. No needles will be used for this test. We will collect images of the carotid artery blood vessel in the neck. Separately, we will also use a large cuff device called a pulse wave analysis system, this will allow us to measure central blood pressure (the actual blood pressure at heart level and not in the arm). This test allows us to see how stiff blood vessels are. For this, we will take some measurements and the cuff will squeeze quickly to get a measurement. We will place a cuff on the arm for measurement and then next place a cuff separately on the leg for a measurement.

Blood Pressure Monitoring appointment*:*

This requires a visit to learn about the ambulatory blood pressure monitor and to get set-up with a cuff and monitor. The total time for this is about 30 minutes. This will occur on UNH campus in NH hall. The system is an at-home blood pressure monitor that is about the size of a cell phone. It will take measurements every half hour during a 12-hour period. While wearing the cuff and monitor, when the pager goes off, they will push the monitor's button to force an automatic blood pressure reading. We will show you how to do this during the visit to the lab. If they are a firefighter, we also ask that they remove the monitor device right before donning fire gear and take the monitor to the call on the apparatus. We ask them to remove it while wearing your gear because monitors will not record blood pressure when you move. This method is effective and has been done in the lab during our studies. This method has also been done in prior cohorts of this study that were completed at other institutions. Once they get back on the apparatus to return to station, we ask them to put the monitor back on and take another manual reading on the way back to station. After that, blood pressure measures will continue to be taken automatically at 30-min intervals.

If they are not a firefighter, we will instruct how to download a mobile app which we will use to randomly page them 1 or 2 times over the 12-hour period. They will also push the monitor's button to force an automatic blood pressure reading.

***Fitness Testing Appointment**:*

The total time for the fitness testing will be around 45 minutes, and each of the tests will measure a part of fitness. This will occur on UNH campus in NH hall or in the firehouse if for convenience the crew would like to meet at the firehouse. We only allow this if the firehouse has a treadmill. This is also allowed since for the safety of the community protected by the fire crew, we need to keep them close to the firehouse in case a 911 call comes in, then they are able to immediately respond. Also, past cohorts of this study have been offered this so to keep the study consistent, this policy will continue. A seated clinical blood pressure measurement will be taken first. The fitness test session includes: plank pose, stairway climb, 12-step climb, right and left single-leg stand, wall sit, and a treadmill test. All tests will be done in civilian fitness clothing.

Plank pose test to assess core strength. Hold plank position until exhaustion or when the position is compromised. Data will include total time.

Stairway climb test to assess leg endurance/strength. Climb up/down stairs for 2 minutes. Data will include total number of steps.

12-step climb test to assess agility and power. Ascend 12 steps as fast as possible. Data will include total time.

Balance test. Stand on single leg while holding a 15 lb dumbbell until exhaustion or balance is lost. This will be repeated with the other leg. Data will include total time.

Wall sit test to assess functional ability and leg strength. Squat down to sitting position with back flat against the wall, legs at 90-degree angle, and knees over the heels. Hold until exhaustion or when position is compromised. Data will include total time.

Aerobic fitness will be measured by an estimated calculation of VO_{2peak}. The protocol used is the Wellness Fitness Iniative protocol, which is a submaximal treadmill test established for firefighters. This protocol is based on the NFPA 1582 *Standard on Medical Requirements for Firefighters and Information for Fire Department Physicians* and the NFPA 1583 *Standard on Health-Related Fitness Programs for Firefighters*. This submaximal test includes minute stages that take the participant to a target heart rate that is calculated based on age. The submaximal heart rate is less than 85% of the age-predicted maximal heart rate, which falls into the ACSM guideline classification for submaximal exercise test. We have found that in the prior cohorts of this study that test time varies between 2 and 20 minutes, depending on fitness of the participant. None of the participants reached 84% of their age-predicted max heart rate during the test, so it remains a submaximal protocol.

Functional strength test. This is a dummy drag (drag a rescue dummy for distance in 30 seconds) which is completed by the firefighters in the study. The civilian population will not complete this test.

6-Week Intervention: Mediterranean Diet Component

***Pre-Intervention Diet Training**:*

The total time for this training appointment will be around 45 minutes. We will issue a study training manual and teach the serving sizes for the food groups in the Mediterranean Diet. For the entire 6-week period, the diet will be followed.

Also, before starting the diet, each participant will write down all the food that is consumed for a 3-day period. This will give us a baseline assessment of how their diet is before they start the study, and this will guide us to the number of serving sizes to prescribe. We only collect 3-day diet once during the study in order to quantify basic caloric consumption.

***Diet Intervention**:*

The Mediterranean diet includes a high consumption of fruits and vegetables, a moderate consumption of fish, nuts, and wine, and a low consumption of red meat and other meat products. Also, olive oil is the principal source of fat instead of other types of oils. We teach them these basics and the manual has many examples.

During the study, all participants will receive the diet information, will have online access to diet information by our website, http://www.theheartlab.org/#dietexercise, will receive weekly educational documents and tips through email, will be provided with informational websites, and receive many lessons on serving size. We also provide all participants with sample serving size containers to get them started.

For the duration of the diet intervention, they will be asked to track their diet and enter serving numbers into our research website each week. The manual and the website have a nice checklist that can be used to track their weekly diet.

Also, the study manual and website have been used for the prior cohorts of data collection for this study.

Here is a quick summary of the number of servings per week they will target and track during each week of the diet intervention (some serving numbers may be reduced based on body size though):

Vegetables = more than 28 per week
Low/Non-Fat Dairy = 14-21 per week
Fish = more than 4 per week
Red Meat = less than 2 per week
Nuts/Healthy Oils = less than 8 per week
Sweets/Processed Food = less than 4 per week
Fruits = more than 21 per week
Grains/Potatoes = 42-49 per week
Poultry = less than 3 per week
Beans = more than 3 per week
Other Fats/Oils = less than 8 per week

6-Week Intervention: Exercise Training Component

The exercise intervention will be self-report. This means that the exercises will be done at home or in the fire house or in a fitness center. All participants are asked to complete the circuit workout 3 times per week for the 6-week period. For the workout, each station below will be done 3 times within each workout, and it should take around 45 minutes. The workout can be done by going through each station and rotate back around 3 times, or the workout can be done by doing each station 3 times and moving on to the next station. Either way that they choose to complete the workout, the amount of work that they will do is the same, so it gives flexibility to pick each time.

Circuit Exercise Stations and Directions:

1. Unsteady Carry – carry 40 lb or an extrication tool for 100 ft (50 ft over and back)
2. Stairway Run/Walk – ascend and descend a stairway continuously for 3-minutes
3. Plank Pose- hold plank pose for 45 seconds. If cannot hold for 45 seconds, hold for as long as possible.
4. Weighted Carry – carry 20 lb or a fireground tool for 100 ft (50 ft over and back), moving as fast as possible.
5. R/L Single Leg Stands – stand on single leg while holding a 15 lb dumbbell or fireground tool for as long as can maintain balance. Repeat with other leg.
6. Stairway Carry – carry 15 lb dumbbell or fireground tool up and down the equivalent of 30 steps.

Post-Intervention Testing Visits

They will complete the exact same tests after the intervention as they did before.

STUDY PERSONNEL

-Deborah Feairheller, PhD, FACSM – Principal Investigator. This proposed intervention has already been completed for several cohorts at my last school, so I have experience with how to manage the trial. I am certified in CPR as a professional rescuer, have completed the IRB Human Subjects training module, have completed BBP training, and completed the HIPAA certificate. I also have been a certified Phlebotomist for years and have completed many trials that involved blood draws.

-Student researchers will be added to the project once they complete the IRB and BBP training modules. Their names will be submitted to the IRB as a modification to this protocol once they are trained. All student researchers will be trained in the methods and will be required to maintain participant privacy. In my research experience, students who work with me do continuous and documented training in all of the laboratory and clinical human research skills.

DATA

Data will be deidentified in study database and when shared with the sponsor. All participants will be assigned an ID code upon entry into the study. All data collection forms will have this ID number listed, with no identifying information at all on the data sheets. We will keep all documentation safely locked in a locked office, in a locked file cabinet. All data points will be entered based on the ID number, and all data will be stored on UNH Box. Only the PI and students affiliated with the study will have access to the data and any data kept on Box will be deidentified.

Data will be aggregated and presented in publications and presentations.

The only form with identifying information will be the Health History form. Upon study completion, any identifying information will be destroyed by shredder. As the study is sponsored by the American Heart Association, the approved data plan states that data will be made available through clinicaltrials.gov.

Our interest is in estimating the effect of exercise and diet on the change in blood pressure surge and examine whether it differs between groups. Quantitative analysis will be done. Data will be expressed as mean ± the standard deviation, and statistical analyses will be performed using SPSS. The distribution of all variables will be examined using the Shapiro-Wilk test of normality. Repeated measures ANOVA will examine whether any condition by time interaction effects exist. Post-hoc within-group analysis will be performed using paired t-tests to compare values between time-

points. Between group analyses will be performed using independent t-tests to determine if there were significant differences between the firefighter and civilian test groups at each time-point. Pearson correlation will determine if there are relationships between variables, which will be further examined by linear regression analysis.

RISKS

The possible **risks**, exactly as described in the consent form, include the following:

Loss of Confidentiality: Once others know that you are participating in the study, you may lose some confidentiality. Fire crews work in close quarters and some spend time living together in the fire house, so confidentiality may be lost by your presence at the testing appointments. We will reduce this risk because your name will not be on any documents and your personal data will not be shown to anyone during the test sessions.

*Depression, Anxiety, and Stress Scales (DASS-21)***:** The risk associated with completing this short 21-item survey is that you may feel uncomfortable while answering the questions. If you feel this and your symptoms are severe, we will work with you to refer you to a proper clinician who is part of your health network.

*Blood glucose, cholesterol, and blood draw***:** These measurements will involve a finger prick and a needle stick. The risks associated are slight discomfort in the site. These are routine and conventional procedures used to measure blood levels of metabolites. Minor risks include a small amount of bleeding under the skin (bruising), but this has been reported in <10% of the cases, dizziness, and a very small risk of infection (1 in 1000). The risk of infection will be reduced by proper cleaning and antiseptic techniques by the technician.

*Blood vessel studies***:** The blood vessel ultrasound studies may include discomfort in the arm and leg when the cuff squeezes to take a measurement. This feeling could be similar to what is felt when a foot or leg falls asleep after sitting in certain positions. This is not a risk to your health, but it is a discomfort. To help with this risk, we recommend that you stay very still and as the blood flows back to the arm and the feeling will go away.

*Fitness testing/training***:** The risk of any exercise is injury to muscles, joints, ligaments, and tendons. It has been found that in 1 out of every 70,000 exercise tests, a person could die from heart problems. In medical terms, doctors call this a rare event. Because you are otherwise healthy with no known risk factors, the risks of a medical problem are even lower. You are aware that if any exercise makes you uncomfortable, you should notify us immediately.

*Diet intervention***:** The risk of allergy exists when any special diet is followed. You are asked in your initial Wellness questionnaire if you have any known food allergies and this is documented in the inside of your folder. If you do have allergies, a modified diet will be provided to you. If something arises, please notify HEART lab staff immediately.

BENEFITS

The possible **benefits**, exactly as described in the consent form, include the following:

By participating in this study it is hoped that you will gain information about your health and fitness levels. You also get to participate in a lifestyle intervention and find how the intervention changes your health. Whether these benefits will occur for you cannot be guaranteed.

Also the broader benefit to the community is great by your participation. Firefighters across the world need to be aware of their blood pressure levels and should know that the blood pressure surge can be large with pager alarm. If this research can identify potential relationships between the blood pressure surge and cardiovascular health, the knowledge could save lives. Also, if this study can show that a simple diet and exercise program can reduce the blood pressure surge, we could save lives.

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