Spring 4-30-2021

The Effect of Chronic Alcohol Consumption on Exercise-Induced Muscle Damage in Young Men

Emma Hamilton
University of Mississippi

Grant Hilliard
University of Mississippi

Follow this and additional works at: https://egrove.olemiss.edu/hon_thesis

Part of the Medicine and Health Commons, Musculoskeletal, Neural, and Ocular Physiology Commons, Musculoskeletal System Commons, Orthopedics Commons, Other Chemicals and Drugs Commons, Other Medicine and Health Sciences Commons, Other Public Health Commons, Sports Sciences Commons, and the Sports Studies Commons

THE EFFECT OF CHRONIC ALCOHOL CONSUMPTION ON

EXERCISE-INDUCED MUSCLE DAMAGE IN YOUNG MEN

by
Grant Hilliard and Emma Hamilton

A thesis submitted to the faculty of The University of Mississippi in partial fulfillment of
the requirements of the Sally McDonnell Barksdale Honors College.

Oxford, Mississippi
May 2021

Approved by

_____
Advisor: Dr. Ling Xin

_____
Reader: Dr. Thomas Andre

_____
Reader: Dr. Matthew Jessee

_____
Reader: Dr. Paul Loprinzi

ACKNOWLEDGEMENTS

ABSTRACT

PURPOSE: To investigate the effects of chronic alcohol consumption on exercise-induced muscle damage of the knee extensors in young men. **METHODS:** Twenty-one males (age 21.9 ± 1.1 yr; weight 183.4 ± 27.6 lbs; height 174.0 ± 13.1 cm) performed 100 maximal eccentric contractions at 30°/sec of the knee extensors using their non-dominant leg. The isometric and isokinetic muscle strengths (60°/sec and 180°/sec) were measured pre-exercise and immediately, 24 h, 48 h, 72 h, 96 h, and 120 h post-exercise. Muscle soreness and plasma creatine kinase (CK) activity were measured pre-exercise and 24 h, 48 h, 72 h, 96 h, and 120 h post-exercise. Data were analyzed using two-way repeated-measures ANOVA to determine the main effects of time (exercise), group (non-drinker vs. frequent drinker), and their interaction terms. **RESULTS:** There were significant main effects of time for isometric strength ($F_{6, 114} = 8.11$, $P < 0.001$), isokinetic strength at both 60°/sec ($F_{6, 114} = 11.02$, $P < 0.001$) and 180°/sec ($F_{6, 114} = 9.88$, $P < 0.001$), muscle soreness ($F_{5, 95} = 26.64$, $P < 0.001$), and plasma CK activity ($F_{5, 70} = 5.15$, $P < 0.001$). There were no significant effects of group or interaction for any of the variables. **CONCLUSION:** There was not an evident effect of chronic alcohol consumption on exercise-induced muscle damage in young men. This may likely be due to the small sample size, the relatively small magnitude of muscle damage, the time of alcohol consumption relative to the bout of exercise, and the between-subjects study design.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF ABBREVIATIONS

EIMD	Exercise-Induced Muscle Damage
DOMS	Delayed-Onset Muscle Soreness
CK	Creatine Kinase
mTOR	Mechanistic Target of Rapamycin
CNTF	Ciliary Neurotrophic Factor
TGFβ1	Transforming Growth Factor Beta 1
TNF-α	Tumor Necrosis Factor Alpha
MRI	Magnetic Resonance Imaging
MVC	Maximal Voluntary Contraction
IRB	Institutional Review Board
V0	Initial Visit
V1-7	Visits 1-7
PAR-Q	Physical Activity Readiness Questionnaire
ND	Non-Drinkers
FD	Frequent Drinkers
NMMC	North Mississippi Medical Center

INTRODUCTION

Eccentric exercise is characterized by a forced lengthening action of skeletal muscle fibers to slow or stop the movement produced by an outside force. This eccentric action results in temporary muscle damage, especially in untrained individuals. Exercise-induced muscle damage (EIMD) is typically measured through indirect markers such as delayed-onset muscle soreness (DOMS), a prolonged loss of muscle force, and an increase in creatine kinase (CK) activity in the blood (Clarkson & Hubal, 2002). Crowell *et al.* (2019) and González-Reimers *et al.* (2014) have shown that alcohol consumption could modify the repair system of damaged skeletal muscle fibers. For example, chronic alcohol consumption has a negative effect on isometric and tetanic twitch force development and muscle fatigability (Crowell *et al.,* 2019). It has also been shown to cause an imbalance in the synthesis and breakdown of muscle proteins and induce apoptosis in damaged skeletal muscle (González-Reimers *et al.,* 2014).

There is existing evidence that an acute moderate dose (1g/kg body weight) of alcohol following a bout of eccentric exercise has a negative effect on muscle recovery after the damaging exercise (Barnes *et al.,* 2010). This post-exercise acute consumption of alcohol has been shown to significantly increase muscle weakness, likely due to a disruption of the repair process of damaged muscle fibers (Barnes *et al.,* 2010). Histological examination of the acute alcoholic myopathy demonstrated necrosis, edema, and inflammation (Rubin *et al.,* 1976). Though the specific mechanisms behind these

negative effects of acute alcohol consumption still warrant further investigation, there is existing research that points to a possible effect of alcohol on regulatory cytokines (Dekeyser *et al.,* 2013).

Our main purpose for conducting this study is that chronic alcohol consumption has been shown to cause skeletal muscle myopathy which, as a result, increases these individuals' risk of injury (Crowell *et al.,* 2019). In addition, to our knowledge, the majority of previous studies investigating the effects of alcohol consumption on exercise-induced muscle damage have focused on the effect of acute alcohol consumption. Therefore, our other purpose for conducting this study was to investigate whether chronic alcohol consumption induces a similar effect on muscle repair in young men. We hypothesized that chronic alcohol consumption would aggravate EIMD in young men, which will be characterized by increased delay-onset muscle soreness, a prolonged loss of muscle force, and increased creatine kinase (CK) activity in the blood.

REVIEW OF LITERATURE

Alcohol consumption has a causal relationship with over 60 medical conditions that accounts for 4% of global disease (Room *et al.,* 2005). Despite the evidence of light to moderate alcohol consumption lowering the risk for coronary heart disease, diabetes, thrombosis, and gallstones, the detrimental effects have been found to outweigh the benefits (Grønbæk, 2009). Whereas the J-shaped all-cause mortality curve relative to alcohol does indicate that there is a lower risk for mortality in the low to moderate alcohol consumption group, it also indicates that heavy drinking results in an increased risk for mortality. Consuming light to moderate amounts of alcohol may lead to alcohol dependency, which often results in detrimental heavy drinking (Grønbæk, 2009). A study by Mukamal and Rimm (2008) found that heavier drinking increases the risk of hypertension, hemorrhagic stroke, and atrial fibrillation. Grønbæk (2009) noted that there was evidence causally relating heavy alcohol consumption to cirrhosis of the liver, dementia, multiple types of cancers, osteoporosis, pancreatitis, and amenorrhea. Specifically, Mukamal and Rimm (2008) found that moderate to heavy alcohol consumption can alter levels of sex steroid hormones, disrupt folate metabolism, and aggravate viral hepatotoxicity, all of which may explain the correlation between alcohol consumption and cancer. In addition to the damage to the hepatic, cardiovascular, skeletal, and endocrine systems, alcohol intoxication may result in accidental injuries (Brick, 2004). Brick (2004) also noted that alcohol may impair recovery from these

injuries sustained. Previous research has zoomed in on not only the body as a whole but specific body systems as well.

Although chronic alcohol consumption is frequently connected to liver cirrhosis, it is suggested that alcohol has an even higher occurrence in disrupting the musculoskeletal system (Rubin *et al.,* 1976). The following studies have shown that alcohol consumption has the potential to modify the repair process of damaged skeletal muscle fibers. Crowell *et al.* (2019) suggested that Type II muscle fibers are the primary skeletal muscle fibers affected by chronic alcohol use. They also found that chronic alcohol consumption negatively affected both isometric and tetanic twitch force development while increasing skeletal muscle fatigability. González-Reimers *et al.* (2014) demonstrated that alcohol consumption caused imbalances in the synthesis and breakdown of muscle proteins. Additionally, researchers believe that alcohol may induce apoptosis in damaged muscle fibers. Steiner and Lang (2014) showed that alcohol decreased the basal rate of protein synthesis in the skeletal muscle of mice. They also showed that alcohol ingestion interfered with the mechanistic target of the rapamycin (mTOR) signaling pathway. Additionally, Dekeyser *et al.* (2013) have shown that the chronic ingestion of alcohol can modify the roles of growth and fibrotic factors such as ciliary neurotrophic factor (CNTF) and transforming growth factor beta 1 (TGFβ1).

Specific mechanisms have been proposed to explain the myopathy caused by chronic alcohol consumption. Subjects with chronic alcoholic myopathy typically present with muscle soreness and potential myoglobin in the urine, along with muscle atrophy and weakness (Rubin *et al.,* 1976). These symptoms may be caused by alterations in the

mitochondria and sarcoplasmic reticulum, and accumulation of lipids (Rubin *et al.,* 1976). González-Reimers *et al.* (2014) found that the main histologic feature of alcoholic myopathy is type II fiber atrophy, primarily caused by a protein synthesis and protein breakdown imbalance. As previously mentioned, Kimball and Lang (2018) found that alcohol consumption decreases mTOR complex 1. This decrease causes hypophosphorylation of downstream proteins that regulate translation, thus interfering with sarcoplasmic and myofibrillar protein synthesis. As shown by Dekeyser *et al.* (2013), the alteration in levels of CNTF and TGFβ1 due to alcohol intake decreased the cross-sectional area of regenerated fibers and increased fibrosis. High tumor necrosis factor alpha (TNF-α) levels found in chronic drinkers increase protein catabolism and impair muscle protein synthesis. This increase in levels of TNF-α impacts regulatory cytokines, which causes a pro-inflammatory response related to the muscle atrophy observed in chronic drinkers. Peripheral polyneuropathy caused by a nutritional deficiency and the direct toxicity of acetaldehyde in alcoholics are also associated with muscle atrophy. This association may be both a direct result of ethanol/acetaldehyde toxicity and ethanol-mediated oxidative stress on the brain and skeletal muscle (González-Reimers *et al.,* 2014).

In addition to the effects of chronic alcohol consumption, research often focuses on acute alcohol consumption. These studies have linked alcoholic muscle weakness with alterations in the motor cortex (Barnes *et al.,* 2011). This acute consumption of alcohol may affect axonal transport and block synaptic potentials in somatic neurons, as well as affecting nicotinic acetylcholine receptors (Barnes *et al.,* 2011). In acute alcohol

myopathy, histological examination of the muscle showed edema, necrosis, and inflammation (Rubin *et al.,* 1976). It has also been noted that acute alcohol consumption post-exercise significantly increased muscle weakness (Barnes *et al.,* 2010). Barnes *et al.* (2010) also found that this is likely due not to a weakening of all skeletal muscles, but rather alcohol disrupting the recovery processes of muscle that has already been damaged.

To the best of our knowledge, no human study has investigated the effects of chronic alcohol consumption on muscle recovery after exercise-induced muscle damage (EIMD). Eccentric exercise has been used as a reliable and effective EIMD model in human studies (Clarkson & Hubal, 2002). Eccentric exercise resulted in prolonged muscle stiffness and soreness in untrained individuals (Proske & Morgan, 2001). The initial event(s) caused by eccentric exercise that likely results in these prolonged effects are the disruption of sarcomeres and damage to the excitation-contraction coupling system, although there is controversy regarding which is the primary event (Proske & Morgan, 2001). Warren *et al.* (1993) found that caffeine, by causing the release of calcium from the sarcoplasmic reticulum, led to a contraction in the damaged muscle of mice. This supports the hypothesis that the excitation-contraction coupling system damage may be the primary point of prolonged damage observed.

Exercise-induced muscle damage can be evaluated by either direct or indirect markers. Direct markers include the myofibrillar disruptions in the damaged muscles. Direct assessment of EIMD is challenging because it can only be realized via muscle biopsies or magnetic resonance imaging (MRI). The limitations of muscle biopsies

include being invasive and having the potential to not represent the entire muscle (Clarkson & Hubal, 2002). Consequently, EIMD is commonly evaluated by indirect markers such as prolonged muscle force loss, increased blood creatine kinase (CK) activity, and delayed-onset muscle soreness, as these markers are easier to obtain and evaluate (Clarkson & Hubal, 2002).

Creatine kinase (CK) is a muscle protein that is commonly released into the blood when muscle damage occurs (Warren *et al.,* 1999), and is thus often used as a marker of muscle damage. Subjects performing intense eccentric contractions are very likely to experience increased CK activity in their blood due to the damage of sarcolemma and Z-disks (Koch *et al.*, 2014). Although CK is frequently measured in EIMD studies, there is high interindividual variability with CK activity. While increased CK activity can be utilized to assess the presence of muscle damage, interindividual variability makes it difficult to quantify the magnitude of muscle damage that has occurred. Various factors have been associated with CK variabilities such as % body fat, sex, genetic factors, ethnicity, and the exercise modality used (Kim & Lee, 2015).

Muscle strength measurements are often taken to assess EIMD. Prolonged muscle force loss measured by the maximal voluntary contraction (MVC) torque is one of the most reliable indirect markers of EIMD in subjects (Warren *et al.*, 1999). Muscle damage directly limits the muscle's ability to contract and produce a force. Therefore, the subject's MVC torque would be expected to decrease after EIMD. Although this mode of measurement is very accurate and reliable, some limitations still exist such as determining the difference between fatigue-related or injury-related reductions in force

measurement and if maximal-effort is given by the subject during measurements (Warren *et al.*, 1999).

Delayed-onset muscle soreness (DOMS) is commonly used in human studies as another indicator of EIMD. Muscle soreness usually appears 24-48 hr post-exercise (Clarkson & Hubal, 2002) and is thought to be attributed to pressure, swelling, histamines, prostaglandins, and bradykinins (Clarkson & Hubal, 2002). Muscle soreness is generally not as reliable as the previous indirect markers (Warren *et al.,* 1999) as it is a subjective measurement and may be due to the inflammation of the connective tissue surrounding the muscle instead of damage to the muscle itself after the exercise has been performed (Nosaka *et al.,* 2002).

To summarize, previous research has demonstrated that there is a significant association between acute alcohol consumption and EIMD, but a correlation with chronic alcohol consumption lacks investigation. There is existing evidence of chronic alcohol consumption disrupting the function of the skeletal system, but it is still unknown if or how this has an effect on muscle damage and recovery from eccentric exercise.

METHODOLOGY

Study Design

The protocol was approved by the University of Mississippi Institutional Review Board (IRB) and written consent was received from each participant. Prior to the start of the study, each participant had an initial visit (V0) in which they signed the consent forms, received a detailed outline of the study timeline, and filled out a Physical Activity Readiness Questionnaire (PAR-Q). The PAR-Q was completed to determine that each subject would be capable of completing the exercise safely. On visit 1 (V1), each subject received baseline measurements of muscle force. During this baseline visit, we also drew the subjects' blood for subsequent CK analysis. The subjects performed the eccentric exercise bout during visit 2 (V2). Additionally, muscle soreness, pre-exercise muscle force, and post-exercise muscle force were accessed in V2. For the five consecutive days following the damaging exercise bout, each visit occurring at the same time, the subjects came in for a blood draw (to be used for CK activity measurement) along with muscle soreness and muscle force measurements (Figure 1).
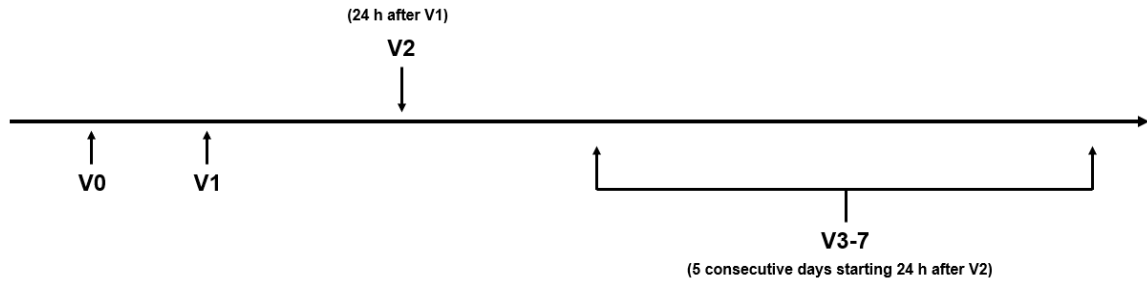
Figure 1: Study Timeline. Visit 0 (V0): informed consent document; visit 1 (V1): familiarization of protocol, baseline muscle force measurement, blood draw; visit 2 (V2): muscle soreness evaluation, pre-exercise muscle force measurement, knee extension eccentric exercise, post-exercise muscle force measurement; visits 3-7 (V3-7): muscle soreness evaluation, muscle force measurement, blood draw.

Participants

Twenty-one males completed all the study visits (age 21.9 ± 1.1 yr; weight 183.4 ± 27.6 lbs; height 174.0 ± 13.1 cm). Of those that completed the study, 1 participant identified as African-American, 4 identified as Asian, 14 participants identified as Caucasian, 1 identified as Hispanic, and 1 identified as other. 19 participants were right-leg dominant and thus exercised their left leg, while the remaining 2 were left-leg dominant and thus exercised their right leg.

Participants were put into categories based on their drinking habits, described as "non-drinker (ND)" or "frequent drinker (FD)," where a frequent drinker was defined as consuming 15 drinks or more every week during the past 12 months. A drink signifies half an ounce of absolute alcohol (e.g. a 12-ounce can or glass of beer or cooler, a 5-ounce glass of wine, or a drink containing 1.5-ounces of liquor). They had to agree to comply with the study conditions and refrain from any strenuous or new physical activity

during participation. Subjects also had to agree to refrain from the use of oral and topical analgesics, heat or cold treatment, physical therapy, massage, or any other muscle treatment, along with consuming cough/cold products during visits 1-7. We also asked that they discontinue supplements on the determination of the investigator that it would influence study results.

Potential subjects were excluded from the study if they had an occupation requiring heavy lifting, had participated in weight training activity of the lower body, or if they had participated in a muscle soreness trial using their legs within the past six months. They were also excluded if they were smokers, were currently taking any medications that would influence study results such as products with analgesic properties, taking supplements over the course of the study, used corticosteroids within the past 8 weeks including topical preparations, or if they consumed any narcotic (e.g. codeine) or illicit drugs (e.g. marijuana) within the previous seven days. Additionally, they could not have undergone orthopedic surgery in the leg (unless cleared by physician) or have any skeletal, muscular, or neuromuscular dysfunction, have any medical condition such as diabetes, hypertension, kidney, cardiovascular, or pulmonary disease, nor be likely to have problems completing the study exercise requirements as deemed by the investigators.

Eccentric Exercise

Subjects performed eccentric exercise of the knee extensors using their non-dominant leg on a Biodex System 3.0 Isokinetic Dynamometer (Biodex Medical Systems, New York, USA). Full knee extension (0°) was entered as a reference value into

the computerized dynamometer system. The starting position was set at 35° of knee flexion. The subjects were instructed to perform 100 maximal isokinetic eccentric contractions of the quadriceps at 30°/sec. The eccentric exercise was divided into 10 sets of 10 repetitions. Subjects were allowed to rest for ten seconds in between each repetition and one minute between each of the sets.

Muscle Force Measurement

The muscle force of the knee extensors was measured using a Biodex System 3.0 Isokinetic Dynamometer. Subjects performed both isometric and isokinetic tests on their nondominant leg during each visit. In the isometric test, the nondominant leg was set at 70° of knee flexion. The subjects performed maximal isometric contractions of the knee extensors for 3 repetitions and were given a one-minute rest period between each of the repetitions. After the 3 repetitions were performed, the subject was instructed to rest for 5 minutes before the isokinetic test was performed. In the isokinetic test, subjects completed 3 maximal contractions at 60°/sec and 3 maximal contractions at 180°/sec. After the 3 maximal contractions at 60°/sec were completed, the subject was given a 2 minute rest period before beginning the 3 maximal contractions at 180°/sec.

Muscle Soreness Evaluation

Subjects completed a pre-exercise soreness/pain assessment using a visual analog scale by marking a vertical line through a 100mm horizontal line after performing two full squats to indicate their peak muscle soreness. The left edge of the line represented no muscle soreness while the right edge represented the highest degree of muscle soreness they had experienced. After the subject marked the line, the distance from the left edge to

the mark made by the subject was recorded. If the muscle soreness measurement at the start of Visit 2 was determined to be 10mm or less in each leg, the subject was allowed to continue the exercise program. If the muscle soreness was greater than 10mm, the subject was instructed to return 2 or more days later to allow any soreness to dissipate.

Plasma Creatine Kinase (CK) Activity

Subjects were seated in a reclining phlebotomy chair, and a tourniquet was placed around the proximal upper extremity approximately 5cm above the humeroulnar and humeroradial articulations. Blood samples were collected from the antecubital vein and were then spun in the centrifuge for 15 min at 3000 rpm to separate the plasma from the other contents of the blood. The plasma samples were stored in the -80°C freezer until ready to transport. After a subject's blood samples were collected from all visits, the plasma samples were packed up and shipped to North Mississippi Medical Center (NMMC) where the CK activity level was analyzed.

Statistical Analysis

Two-way repeated-measures ANOVA was used to determine the main effects of time (exercise), group (non-drinker vs. frequent drinker), and their interaction terms. The CK data were not normally distributed and thus were log10 transformed prior to performing the repeated measures ANOVA. A significance level was set at $P < 0.05$. All the data analyses were conducted using JASP (Version 0.14.1) statistical software (https://jasp-stats.org/).

RESULTS

Isometric Peak Torque

Isometric peak torque was normalized over the baseline value and expressed as a percentage change (Figure 2). There was a significant main effect of time ($F_{6, 114} = 8.11$, P < 0.001), indicating a reduction in the isometric strength after the eccentric exercise. Maximal isometric muscle force loss occurred immediately post-exercise for both non-drinkers (-15.3 ± 18.1%) and frequent drinkers (-17.2 ± 15.5%). The isometric peak torque returned to the pre-exercise value at 72 h post-exercise for heavy drinkers and 96 h post-exercise for non-drinkers. However, there was no significant main effect of group ($F_{1, 19} = 0.22$, P = 0.64) or interaction effect. ($F_{6, 114} = 0.59$, P = 0.74).
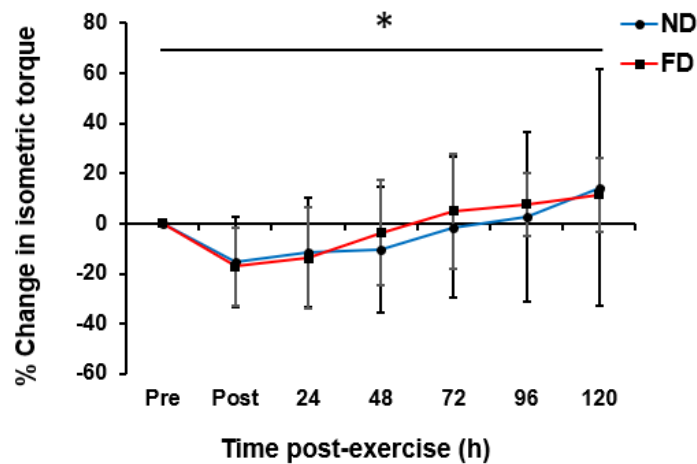

Figure 2. Isometric peak torque before exercise (Pre) and immediately (Post), 24 h, 48 h, 72 h, 96 h, and 120 h post-exercise after eccentric exercise. Data values are mean ± SD; n

= 11 for frequent drinkers (FD) and n = 10 for non-drinkers (ND) for each time point. *

indicates a significant main effect of time.

Isokinetic Peak Torque (60 and 180°/sec)

Isokinetic peak torque at 60 and 180°/sec were normalized over baseline values

and presented as a percentage change in Figure 3 and 4, respectively. There were

significant main effects of time for the isokinetic strength at both 60°/sec ($F_{6, 114}$ = 11.02,

P < 0.001) and 180°/sec ($F_{6, 114}$ = 9.88, P < 0.001), indicating a reduction in the isokinetic

strength after the eccentric exercise. The maximal loss of isokinetic (60°/sec) muscle

force occurred immediately post-exercise for both non-drinkers (-22.7 ± 11.3%) and

frequent drinkers (-22.0 ± 16.7%). The maximal loss of isokinetic (180°/sec) muscle

force occurred immediately post-exercise for non-drinkers (-17.8 ± 15.1%) and 24 h

post-exercise for frequent drinkers (-13.6 ± 22.1%). The isokinetic (60°/sec) peak torque

returned to the pre-exercise value at 72 h post-exercise for both non-drinkers and frequent

drinkers. The isokinetic (180°/sec) peak torque returned to the pre-exercise value at 48 h

post-exercise for non-drinkers and 72 h post-exercise for frequent drinkers. However,

there were no significant main effects of group ($F_{1, 19}$ = 0.05, P = 0.82 for 60°/sec; $F_{1, 19}$ =

0.01, P = 0.93 for 180°/sec) or interaction effects ($F_{6, 114}$ = 0.16, P = 0.99 for 60°/sec; $F_{6, 114}$ = 0.21, P = 0.97 for 180°/sec).

Figure 3. Isokinetic peak torque at 60°/sec before exercise (Pre) and immediately post (Post), 24 h, 48 h, 72 h, 96 h, and 120 h post-exercise after eccentric exercise. Data values are mean ± SD; n = 11 for frequent drinkers (FD) and n = 10 for non-drinkers (ND) for each time point. * indicates a significant main effect of time.
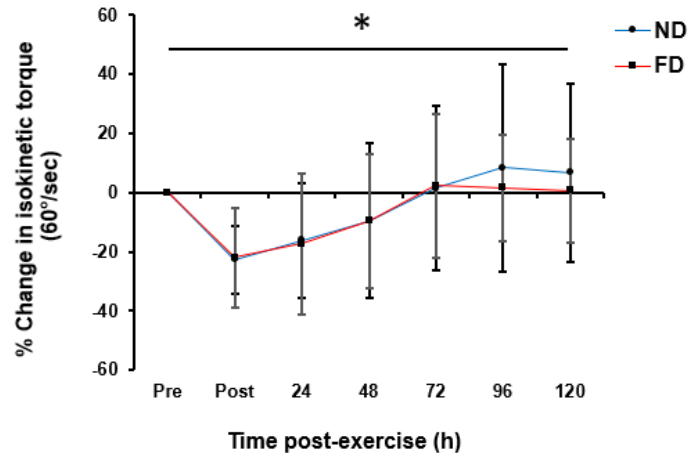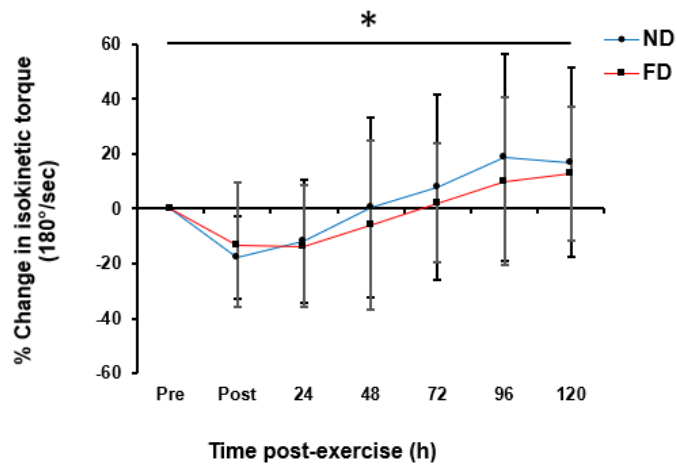

Figure 4. Isokinetic peak torque at 180°/sec before exercise (Pre), immediately post (Post), 24 h, 48 h, 72 h, 96 h, and 120 h post-exercise after eccentric exercise. Data values are mean ± SD; n = 11 for frequent drinkers (FD) and n = 10 for non-drinkers (ND) for each time point. * indicates a significant main effect of time.

Muscle Soreness

There was a significant main effect of time ($F_{5, 95} = 26.64$, $P < 0.001$), indicating an increase in muscle soreness after the eccentric exercise (Figure 5). Peak muscle soreness occurred at 48 h post-exercise for both non-drinkers (32.1 ± 21.6mm) and frequent drinkers (36.7 ± 25.2mm). However, there was no significant main effect of group ($F_{1, 19} = 0.63$, $P = 0.44$) or interaction effect ($F_{5, 95} = 0.12$, $P = 0.99$).
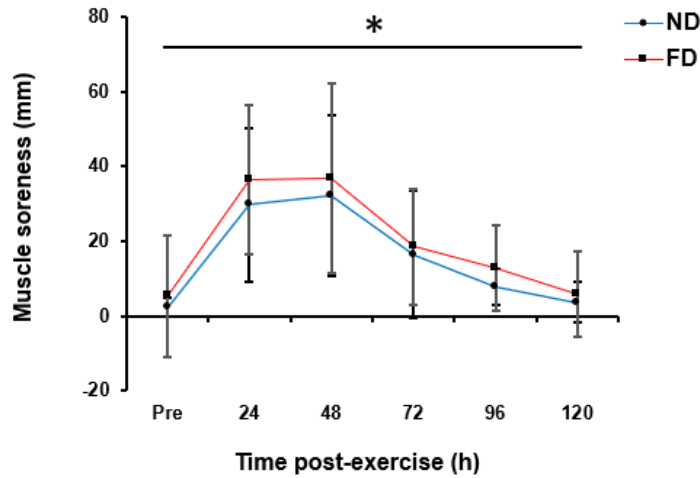

Figure 5. Muscle soreness before exercise (Pre) and 24 h, 48 h, 72 h, 96 h, and 120 h post-exercise after eccentric exercise. Data values are mean $\pm$ SD; n = 11 for frequent drinkers (FD) and n = 10 for non-drinkers (ND) for each time point. * indicates a significant main effect of time.

Plasma CK Activity

Plasma CK activity peaked at 24 h post-exercise for both non-drinkers (2.4 ± 0.3 U/L) and frequent drinkers (2.5 ± 0.3 U/L) (Figure 6). There was a significant main effect of time ($F_{5, 70} = 5.15$, $P < 0.001$). However, there was no significant main effect of group ($F_{1, 14} = 0.06$, $P = 0.81$) or interaction effect ($F_{5, 70} = 0.26$, $P = 0.94$).
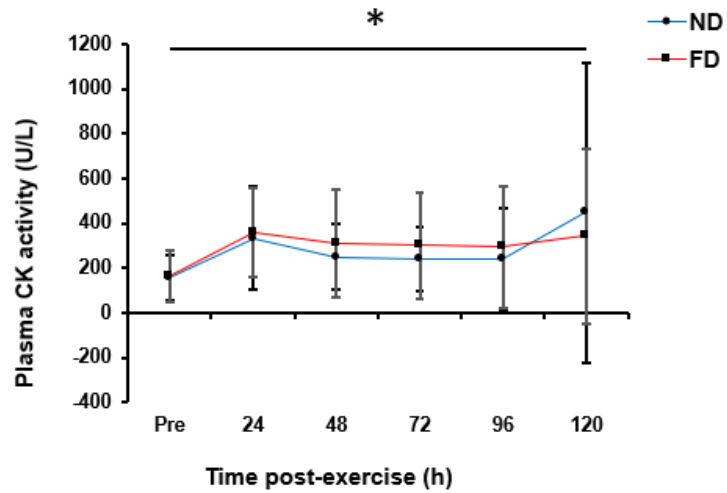
Figure 6. Plasma creatine kinase (CK) activity before exercise (Pre) and 24 h, 48 h, 72 h, 96 h, and 120 h post-exercise after eccentric exercise. Data values are mean ± SD; n = 8 for frequent drinkers (FD) and n = 8 for non-drinkers (ND) for each time point. * indicates a significant main effect of time.

DISCUSSION

The primary objective of this study was to investigate whether chronic alcohol consumption has an effect on exercise-induced muscle damage (EIMD) in young men. Overall, the results did not indicate that chronic alcohol consumption impacts EIMD in young men. There were no significant differences in all the outcome measures (isometric peak torque, isokinetic peak torque, CK activity, and muscle soreness) between frequent drinkers and non-drinkers.

In this study, we utilized indirect markers frequently used in studies regarding EIMD, including muscle force, muscle soreness, and blood CK activity. We observed a significant main effect of time for all the outcome measures, providing strong evidence that the eccentric exercise protocol used in this study was successful in inducing muscle damage.

Previous studies (Rubin *et al.,* 1976; Crowell *et al.,* 2019; Gonzalez-Reimers *et al.,* 2014; Steiner & Lang 2014; Dekeyser *et al.,* 2013) have demonstrated that chronic alcohol consumption may modify the repair process of damaged muscle fibers, cause an imbalance between the synthesis and breakdown of muscle proteins, result in apoptosis, decrease the basal rate of protein synthesis, and modify the roles of growth and fibrotic factors. These studies would suggest that chronic alcohol consumption may also impact EIMD, as this study analyzed. Further, Barnes *et al.* (2010) have found that an acute dose

of alcohol post-exercise resulted in a significant increase in muscle weakness, though that did not seem to be present in our investigation of chronic alcohol consumption.

The data of the current study failed to support our hypothesis that chronic alcohol consumption would impose an effect on EIMD in young men. There was no significant effect of group or interaction term for all variables. Though frequent drinkers seemed to have higher levels of muscle soreness over an extended period of time, these results were not statistically significant. One possible explanation for this lack of evidence of an effect of chronic alcohol consumption on EIMD could be the time of alcohol ingestion. Previous studies by Barnes *et al.* (2010) demonstrated a significant difference in maximal isokinetic and isometric torque between groups when one group was given a dose of alcohol immediately following eccentric exercise. Our study did not analyze the time of alcohol consumption within the frequent drinker group, so it is unknown whether alcohol was consumed before or after the eccentric exercise, nor how many hours after the exercise bout. Therefore, it is possible that the effect of alcohol is dependent on time ingested relative to eccentric exercise and not on the chronic consumption of alcohol. To further support this, Clarkson & Reichsman (1990) found that alcohol consumed prior to exercise has no significant effect on muscle damage. Due to this, there is the possibility that the subjects consumed alcohol prior to the eccentric exercise bout rather than post-exercise, which would likely pose this same effect and contribute to our lack of significant findings.

In addition to the possible effect of the time of alcohol consumption on EIMD, previous studies showing success in the effect of acute alcohol consumption on muscle

damage included 300 maximal eccentric contractions in their eccentric exercise protocol, compared to our 100 contractions (Barnes *et al.,* 2010). Additionally, Barnes *et al.* (2010) noted a loss in muscle strength of up to 40%, whereas the current study only observed about a 20% muscle strength loss. Clarkson & Hubal (2002) further supports this by stating that maximal eccentric exercise can often produce up to a 50-65% loss in muscle force. Barnes *et al.* (2010) also used subjects who participated in resistance training on a regular recreational basis, whereas we recruited sedentary subjects. This may have contributed to the short falling in muscle damage production. Therefore, it is possible that our exercise protocol failed to induce enough muscle damage to the quadriceps of the young men in our study to successfully demonstrate the detrimental effects of chronic alcohol consumption on muscle damage. We chose to use a lower amount of eccentric contractions due to our recruitment of sedentary individuals, as we did not want to risk overexerting them. However this did not appear to be an issue, so an increase in repetitions during the eccentric exercise bout may be beneficial in inducing a greater amount of muscle damage, regardless of training status, which may help accentuate the results to see statistical significance.

Whereas some previous studies (Barnes *et al.,* 2010; Levitt *et al.,* 2017; McLeay *et al.,* 2017) investigated the alcohol effects on muscles using within-subject study designs, the current study was performed via a between-subject design. This imposes a possible limitation, as the intersubject variability might have weakened the capacity of the study to identify the potential effect of alcohol consumption. Therefore, comparing between groups rather than within-subjects may affect the results and could factor into

why the current study failed to recognize a significant effect of chronic alcohol consumption on EIMD.

Due to the current COVID-19 pandemic, we were forced to end trials early. As a result of this, we were not able to recruit as many subjects as we had originally intended. This sample size limitation could also potentially impact our data, resulting in a lack of statistically significant findings.

The design of this study also imposed a self-report limitation, as we were not able to verify that the subjects were truly frequent drinkers or non-drinkers and simply went off of their reports. In addition, the frequent drinkers only reported that they drank 15 or more drinks a week. Therefore, we do not know exactly how many each subject typically consumed. This could enhance the variability in our findings, based on if the subject consumed 15, 20, 30, etc. drinks per week. Finally, we did not note the pattern of alcohol intake by the frequent drinkers group. Some participants may consume 2-3 drinks per day while others may binge drink on the weekends; the latter may be the more likely pattern given our recruitment of college-aged males. This could further enhance the variability in our findings, while also possibly explaining the lack of significant main effect of group or interaction effect. If the subjects were more prone to binge drinking on the weekends, it is possible that the alcohol was completely out of their systems during the weekdays when most of the testing took place.

Going forward, we would suggest that future studies implement a longitudinal study design to investigate the effects of chronic alcohol consumption on EIMD. Indeed, some animal studies have used a longitudinal study design to uncover the chronic alcohol

consumption effects (Dekeyser *et al.,* 2013; McCarthy *et al.,* 2018). However, there may be many drawbacks and limitations to this design for human studies. To conduct longitudinal studies on the effect of chronic alcohol consumption in humans, lifelong abstainers from alcohol would have to be initially recruited, then asked to consume at least 15 drinks a week for an extended period of time, which runs into ethical issues. In addition, long-term frequent drinkers would need to be recruited and then become sober for an extended period of time before retesting. Though this would be a more ethical option, both would need to be tested in order to eliminate the possibility of the long-term effects of alcoholism on EIMD. As a simpler option, we would also recommend using the same design as the current study, but recruiting more subjects to reach statistical power.

CONCLUSION

There was no apparent effect of chronic alcohol consumption on EIMD. This is likely due to the short-falling of the eccentric exercise protocol to induce enough muscle damage to the quadriceps to see the effect, the time of alcohol consumption relative to the bout of exercise, the between-subject design, and/or the sample size and self-report limitations. Future studies are warranted to further investigate the effect of chronic alcohol consumption on EIMD using a more damaging eccentric exercise protocol with an increased number of repetitions, more subjects, or, if possible, a longitudinal study.

LIST OF REFERENCES

Barnes, M. J., Mündel, T., & Stannard, S. R. (2010). Acute alcohol consumption
aggravates the decline in muscle performance following strenuous eccentric
exercise. *Journal of science and medicine in sport*, *13*(1), 189–193.
https://doi.org/10.1016/j.jsams.2008.12.627

Barnes, M. J., Mündel, T., & Stannard, S. R. (2011). A low dose of alcohol does not
impact skeletal muscle performance after exercise-induced muscle damage.
European journal of applied physiology, *111*(4), 725–729.
https://doi.org/10.1007/s00421-010-1655-8

Barnes, M. J., Mündel, T., & Stannard, S. R. (2010). Post-exercise alcohol ingestion
exacerbates eccentric exercise induced losses in performance. *European journal
of applied physiology*, *108*(5), 1009–1014.
https://doi.org/10.1007/s00421-009-1311-3

Brick, J. (2004). Medical Consequences of Alcohol Abuse. *Handbook of the medical
consequences of alcohol and drug abuse* (p. 7–47). Haworth Press.

Clarkson PM, Reichsman F. (1990). The effect of ethanol on exercise-induced muscle
damage. J Stud Alcohol 1990;51:19–23.

Clarkson, P. M., & Hubal, M. J. (2002). Exercise-induced muscle damage in humans. *American Journal of Physical Medicine & Rehabilitation, 81*(Supplement). doi:10.1097/00002060-200211001-00007

Crowell, K. T., Laufenberg, L. J., & Lang, C. H. (2019). Chronic Alcohol Consumption, but not Acute Intoxication, Decreases In Vitro Skeletal Muscle Contractile Function. *Alcoholism, clinical and experimental research*, *43*(10), 2090–2099. https://doi.org/10.1111/acer.14179

Dekeyser, G. J., Clary, C. R., & Otis, J. S. (2013). Chronic alcohol ingestion delays skeletal muscle regeneration following injury. *Regenerative medicine research*, *1*(1), 2. https://doi.org/10.1186/2050-490X-1-2

González-Reimers, E., Santolaria-Fernández, F., Martín-González, M. C., Fernández-Rodríguez, C. M., & Quintero-Platt, G. (2014). Alcoholism: a systemic proinflammatory condition. *World journal of gastroenterology*, *20*(40), 14660–14671. https://doi.org/10.3748/wjg.v20.i40.14660

Grønbaek, M. (2009). The positive and negative health effects of alcohol- and the public health implications. *Journal of Internal Medicine*, 265(4), 407-420. doi:10.1111/j.1365-2796.2009.02082.x

Kim, J., & Lee, J. (2015). The relationship of creatine kinase variability with body composition and muscle damage markers following eccentric muscle

contractions. *Journal of Exercise Nutrition and Biochemistry, 19*(2), 123-129.
doi:10.5717/jenb.2015.15061910

Kimball, S. R., & Lang, C. H. (2018). Mechanisms Underlying Muscle Protein Imbalance
Induced by Alcohol. *Annual review of nutrition*, *38*, 197–217.
https://doi.org/10.1146/annurev-nutr-071816-064642

Koch, A., Pereira, R., Machado, M. (2014). The Creatine Kinase Response to Resistance
Exercise. *Journal of Musculoskeletal and Neuronal Interactions, 14*(1), 68-77.

Levitt, D. E., Luk, H. Y., Duplanty, A. A., McFarlin, B. K., Hill, D. W., & Vingren, J. L.
(2017). Effect of alcohol after muscle-damaging resistance exercise on muscular
performance recovery and inflammatory capacity in women. *European journal of
applied physiology*, *117*(6), 1195–1206.
https://doi.org/10.1007/s00421-017-3606-0

McCarthy, G. M., Farris, S. P., Blednov, Y. A., Harris, R. A., & Mayfield, R. D. (2018).
Microglial-specific transcriptome changes following chronic alcohol
consumption. *Neuropharmacology, 128*, 416-424.
doi:10.1016/j.neuropharm.2017.10.035

McLeay, Y., Stannard, S. R., Mundel, T., Foskett, A., & Barnes, M. (2017). Effect of
Alcohol Consumption on Recovery From Eccentric Exercise-Induced Muscle
Damage in Females. *International Journal of Sport Nutrition and Exercise
metabolism*, *27*(2), 115–121. https://doi.org/10.1123/ijsnem.2016-0171

Mukamal, K. J., & Rimm, E. B. (2008). Alcohol Consumption: Risks and Benefits. *Current Atherosclerosis Reports, 10*(6), 536-543. doi:10.1007/s11883-008-0083-2

Nosaka, K., Newton, M., & Sacco, P. (2002). Delayed-onset muscle soreness does not reflect the magnitude of eccentric exercise-induced muscle damage. *Scandinavian Journal of Medicine & Science in Sports, 12*(6), 337-346. doi:10.1034/j.1600-0838.2002.10178.x

Proske, U., & Morgan, D. L. (2001). Muscle damage from eccentric exercise: mechanism, mechanical signs, adaptation and clinical applications. *The Journal of Physiology, 537*(Pt 2), 333–345. https://doi.org/10.1111/j.1469-7793.2001.00333.x

Room, R., Babor, T., & Rehm, J. (2005). Alcohol and public health. *The Lancet, 365*(9458), 519-530. doi:10.1016/s0140-6736(05)17870-2

Rubin, E., Katz, A. M., Lieber, C. S., Stein, E. P., & Puszkin, S. (1976). Muscle damage produced by chronic alcohol consumption. *The American Journal of Pathology, 83*(3), 499–516.

Steiner, J. L., & Lang, C. H. (2014). Alcohol impairs skeletal muscle protein synthesis and mTOR signaling in a time-dependent manner following electrically stimulated muscle contraction. *Journal of Applied Physiology (Bethesda, Md.: 1985), 117*(10), 1170–1179. https://doi.org/10.1152/japplphysiol.00180.2014

Warren, G. L., Lowe, D. A., & Armstrong, R. B. (1999). Measurement tools used in the

    study of eccentric contraction-induced injury. *Sports Medicine (Auckland, N.Z.)*,

    27(1), 43–59. https://doi.org/10.2165/00007256-199927010-00004

Warren, G. L., Lowe, D. A., Hayes, D. A., Karwoski, C. J., Prior, B. M., & Armstrong, R.

    B. (1993). Excitation failure in eccentric contraction-induced injury of mouse

    soleus muscle. *The Journal of Physiology*, *468*, 487–499.

    https://doi.org/10.1113/jphysiol.1993.sp0197