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Nutraceuticals & Resistance Exercise Training:Effects on Rate Pressure Product--- An Index of Myocardial Oxygen Consumption

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NUTRACEUTICALS & RESISTANCE EXERCISE TRAINING: EFFECTS ON RATE PRESSURE PRODUCT--- AN INDEX OF MYOCARDIAL OXYGEN CONSUMPTION

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ABSTRACT

The primary purpose of this dissertation was to investigate the acute effect of different REs on the heart, the effect of conventional RE on the heart in combination with nutraceuticals, through measuring rate pressure product (RPP). Three studies were conducted in this dissertation.

The first study was to examine the effect of volume-matched single-set and multiple-set leg press exercise on myocardial energy expenditure. Fourteen healthy untrained college students performed 4 sets of 10 repetitions or 40 repetitions of leg press exercise at 150% body weight on different days. Post-exercise RPP, RPP_{diff}, RPP_{perc}, and HR_{perc} for single-set were significantly greater than that of multiple-set RE. These results imply single-set RE exerts a greater stress on the heart. Thus, single-set and multiple-set RE can be prescribed to different populations with varied training goals.

The second study was to investigate the effect of Muscle Sentry® on improving work performance and cardiovascular efficiency. Twenty-one college students performed 3 sets to failure chest and leg pressure exercises at 8 RM with 2 min rest between sets. No treatment effect was found on total work performed and estimated MVO_2 between treatments. These results show Muscle Sentry® intake 40 min prior to doing RE had no effect upon either total lift numbers or estimated MVO_2, and suggests that the benefits of Muscle Sentry® are less than those claimed by the manufacturer.

The final study was to investigate the acute effect of N-acetylcysteine (NAC) on cardiovascular responses to regular RE. Nine recreationally strength trained college students finished this study, NAC or placebo, at a dosage of 1800 mg, was administrated one hour prior to

perform 6 regular REs with 3 sets of 10 repetitions at 80% 1RM, 2 min rest between sets and exercises. No significant difference of post-exercise RPP between both treatments, post-exercise RPP of regular RE was significant greater than that of 1RM test. Increased HR was significant greater in regular RE than that of 1RM test. These results suggest NAC does not reduce post-exercise RPP in a conventional RE training program, HR not SBP plays a vital role in increasing heart stress during conventional RE.

CHAPTER 1. INTRODUCTION

Resistance exercise (RE) is widely accepted as an important method in improving muscle mass and strength. In 1990, the American College of Sports Medicine (ACSM) first recognized resistance training as a significant component of a comprehensive fitness program for healthy adults of all ages (Pollock et al., 2000). Further, the American Heart Association (AHA) updated two scientific statements on the recommendation of RE and cardiovascular disease (Pollock et al., 2000; Williams et al., 2007). Thereafter, RE was applied to a variety of populations and for different treatment goals. However, RE is not always beneficial given that a forceful activity can acutely and rapidly increase the risk of sudden cardiac death or myocardial infarction in susceptible persons (Thompson et al., 2007), and high-level RE is associated with abrupt and large pressure responses (MacDougall et al., 1985). Moreover, RE has been shown to reduce arterial compliance, both for strength-trained athletes and young regular resistance training participants (Bertovic et al., 1999; Miyachi et al., 2004). Thus, RE, especially extreme intense RE, increases the risk of developing adverse cardiovascular events, which leads to a rising interest in examining the heart response to RE.

Maximal oxygen uptake (VO_{2max}) is generally accepted as the best measure of the functional limit of cardiovascular system (Rowell, 1974), while, myocardial oxygen consumption (MVO_2) is a measure of the total energy utilization of the heart (Sonnenblick et al., 1968), and is the product of myocardial blood flow and the difference in oxygen content between aorta and coronary sinus (Nelson et al., 1974). However, VO_{2max} and MVO_2 do not necessarily change in parallel with various exercises (Nelson et al., 1974), and the onset of angina is determined by the work of the myocardium and not by the work of skeletal muscles (Robinson, 1967). These results suggest MVO_2 is a better index for heart stress than VO_{2max}. Though direct

measurement of MVO_2 is accurate, it requires cardiac catheterization and is not feasible for general applications (Nelson et al., 1974). Therefore, the rate pressure product (RPP), a product of SBP and HR, is a surrogate marker for MVO_2 (Tousoulis, 2017), its correlation coefficient to MVO_2 can be as high as 0.92 (Baller et al., 1980). Therefore, RPP was used in this dissertation to examine RE stress on the heart.

Heart disease is much more prevalence in western countries (Kannel, 2000), many treatments have been examined the effect on the heart. Aside from using traditional drugs, emerging research conducted on many nutraceuticals, such as hawthorn, coenzyme Q10, L-carnitine, D-ribose, Carnosine, Vitamin D, some probiotics, Omega-3 and beet nitrates have been found to be associated with improvements in some of the functional parameters in heart failure patients (FG Cicero & Colletti, 2017). Coenzyme Q10, carnitine, taurine, and thiamine together improve heart function (Jeejeebhoy & Sole, 2001), and fish oil may reduce both whole-body and myocardial O_2 demand during exercise, without a decrement in performance (Peoples et al., 2008). In addition, American ginseng has been shown to improve cardiac performance both chronically (Chen, 1996; Toh, 1994) and acutely (Jiang et al., 2014), and beetroot decreased BP and O_2 cost in submaximal exercise (Bailey et al., 2010; Ormsbee et al., 2013). To this point, if these nutraceuticals do work to improve heart function, they might reduce the stress effect RE exerts on the heart.

Even though, previous studies found acute RE increased RPP (Maior et al., 2014; Nogueira et al., 2007), these results were based on either a single set of RE or a simple RE workout that is not regularly performed, not much is known about the acute effect of conventional RE on the heart. Therefore, the purpose of this dissertation was through examining

RPP to investigate the effect of different types of conventional RE on the heart, and RE stress effect on the heart when in combination with nutraceuticals.

Debates, which related to the effect of single- and multiple-set RE on muscular adaptations, have been conducted for decades without a well-accepted consensus as to whether single-sets or multiple-set are superior for optimizing training outcomes (Galvao & Taaffe, 2005; Galvão & Taaffe, 2004). A study finding a relationship between single-set and multiple-set RE on heart stress, could help participants choose wisely between these two exercises. The first study (Chapter 2) was to examine the effect of volume-matched single-set and multiple-set leg press exercise on myocardial energy expenditure.

Supplements are widely used in recreational and professional participants, however, their claimed benefits are hardly to test. Muscle Sentry® claims to improve work performance and cardiovascular efficiency for an acute bout exercise, which fits into our research interest. The second study (Chapter 3) was designed to investigate acute effect of Muscle Sentry® effect on work performance and estimated cardiac energy expenditure.

The third and final study (Chapter 4) was designed to investigate the acute effect of N-acetylcysteine (NAC) on cardiovascular responses to conventional RE. RE has been recognized to increase the workload of the heart (DeVan et al., 2005), while NAC has been showed to improve ejection fraction without affecting blood pressure (Crespo et al., 2011). Thus, if heart workload reduces when performing conventional RE treated with NAC, this could improve the benefits of RE to a great extent.

Ultimately, the research completed throughout this dissertation focused on different types of RE on heart stress and the effect of nutraceuticals on heart stress exerted by conventional RE. The research presented valuable information about the stress RE on the heart, provided guidance

for exercise scientists to develop a suitable RE program for the participants individually. The following chapters detail each experiment individually and a general conclusion is included thereafter.

CHAPTER 2. MYOCARDIAL ENERGY EXPENDITURE INCREASES MORE IN A SINGLE SET OF LEG PRESS COMPARED TO VOLUME-MATCHED MULTIPLE SETS IN UNTRAINED YOUNG ADULTS

2.1 Introduction

Resistance training has become one of the most popular forms of exercise for developing musculoskeletal fitness and overall health, as it can develop strength and cardiovascular fitness, especially when combined with classical endurance exercise (Lamotte et al., 2010). When planning resistance exercise (RE), many variables can all be manipulated to meet certain training goals (de Salles et al., 2010), with the most often manipulated variables being the load, number of sets, number of repetitions completed, and rest periods allotted (Fleck & Kraemer, 1997). However, in addition to adjusting these acute RE variables to achieve certain training goals, safety should also be considered when designing and implementing RE programs. For example, it should be considered how RE can affect the cardiovascular system. For instance, study has shown that RE can reduce arterial compliance (Miyachi et al., 2004), which could be problematic for populations who already have arterial compliance issues. Also, performing heavy resistance training exercises is associated with abrupt and large blood pressure responses that are likely unwarranted for individuals who already have high blood pressure (MacDougall et al., 1985). In either case, the dynamic yet forceful nature of RE results in acute (Battazza et al., 2014), and chronic (Sugawara et al., 2012) pressor responses, which should be monitored during RE, especially for at-risk exercisers.

Ideally, myocardial oxygen consumption (MVO_2), which is a measure of total energy utilized by the heart, can be measured during exercise to determine the increased metabolic demand that exercise places on the heart. However, due to the invasive direct measurement of

MVO_2, it is not feasible for general applications (Nelons et al., 1974). To counter this impracticability, the rate pressure product (RPP), a product of systolic blood pressure (SBP) and heart rate (HR), which is highly correlated to MVO_2 with a correlation coefficient as high as 0.92 (Baller et al., 1980), is a sensitive index of MVO_2 that can be used in practice. This has led to RPP being widely used in clinical areas, both for the prediction of heart diseases (Rafie et al., 2008) and guidance for the rehabilitation process (Villella et al., 1999) where RE may be present.

A considerable amount of research has investigated the myocardial and cardiovascular responses to RE (Battazza et al., 2014; Iglesias-Soler et al., 2015; Río-Rodríguez et al., 2016; Silva et al., 2007), with some research specifically focusing on the work-to-rest ratio (Iglesias-Soler et al., 2015), length and durations of rest periods, and the like (Río-Rodríguez et al., 2016). Thus, in order to optimize RE prescription in terms of the cardiovascular and myocardial responses, simply changing the number of sets (e.g. a single-set or multiple-sets) may have different outcomes. Debates, which related to the effect of single- and multiple-set RE on muscular adaptations, have been conducted for decades without a well-accepted consensus as to whether single-sets or multiple-set are superior for optimizing training outcomes. Some authors have pointed out that single-set RE is more time efficient and equally effective as multiple sets for increasing muscle strength and muscle hypertrophy (Galvão & Taaffe, 2004), while others have demonstrated greater strength gains with multiple-set RE (Galvao & Taaffe, 2005). Regardless of the number of sets performed, the performance differences between protocols are mainly ascribed to different total volumes used, both in the studies supporting single-set (Wolfe et al., 2004) and multiple-set RE (Rhea et al., 2002). Therefore, as it appears as though neither single sets nor multiple sets are clearly more beneficial than the other for improving

performance, it may be wise to consider which is safer in terms of the myocardial or cardiovascular responses.

This leads to the question of how volume-matched single- and multiple-set RE affect acute cardiac stress. However, few studies have been conducted in this area. Therefore, the impact of volume-matched single- and multiple-set RE on the metabolic and oxygen demands should be examined to determine if they have different impacts. Moreover, in many studies, subjects were resistance-trained (Mayo et al., 2016; Río-Rodríguez et al., 2016), which provide valuable information but only for that specific population. Therefore, as there are no studies investigating the acute cardiac stress of RE on untrained subjects, who form the basis for the popularity of single-set training among general fitness enthusiasts (Feigenbaum & Pollock, 1999), the purpose of this study was to examine the effect of volume-matched single-set and multiple-set of RE on the cardiac muscle metabolism with untrained subjects, by measuring RPP. We hypothesized that volume-matched single-set RE would exert more metabolic stress on the heart as compared to multiple-set RE.

2.2 Methods

2.2.1 Study design

Subjects visited the laboratory on four separate occasions, at the same time of the day, separated by a minimum of 48 hours. During each session, they performed the horizontal leg press exercise with either multiple-sets (two individual visits) or a single-set (two individual visits) in a counterbalanced fashion. Upon arriving to the laboratory, subjects quietly rested on the horizontal leg press machine (Body Masters CX 122, Body Masters Sports Industries Inc., Rayne, LA 70578, USA) for 15 minutes. Then, SBP and HR were measured on the left upper arm using a previously-validated automated blood pressure measuring device (Heinemann et al.,

2008) (Omron BP710, Omron Healthcare, Inc., Bannockburn, IL, USA), eliminating inter-technician variability, technician digit preference, and auditory acuity (Pannarale et al., 1993). The multiple-set protocol included 4 sets of 10 repetitions with a load of 150% body mass, and 3 min rest between sets. The single-set protocol was volume-matched and included 40 consecutive repetitions with a load of 150% body mass. Post-exercise SBP and HR were tested immediately after the last repetition of exercise with the same process as the pre-exercise tests. The RPP was then calculated as SBP × HR × 10^{-3} mm Hg · beat · min^{-1}, the RPP_{diff} was calculated as post-exercise RPP minus pre-exercise, and RPP_{perc} was calculated as percentage of RPP change from pre- to post-exercise. The average two trials' parameters for each exercise were used to compare the difference between exercise protocols.

2.2.2 Subjects

This study involved 14 healthy, normotensive (<120/80 mm Hg), untrained college students (5 males, 9 females; 21.14 ± 0.77 years). All subjects had not participated in a structured RE training or aerobic exercise training program for at least 6 months and were asked to maintain their normal daily activity throughout this study. Untrained individuals were chosen as this group has greater risks associated with initiating a training program, and thus have a greater need for information on differences in cardiac stressors. The following additional exclusion criteria were used: a) use of drugs that could affect the cardiovascular responses; b) problems that could impair the execution of the resistance exercises; c) systemic hypertension (≥140/90 mm Hg); and d) usage of supplementations or medications with potential effects on physical performance. Each subject was required to fill out the Physical Activity Readiness Questionnaire (PAR-Q) (Shephard, 1988), and any subject who answered one of the questions with "yes", was excluded from the study. Coffee, tea, alcohol, tobacco intake, or any other substance that is

known to affect HR or blood pressure was prohibited for 48 hours prior to testing as well as avoidance of any formal and strenuous exercise. This study was approved by the Institutional Review Board (IRB) of the Louisiana State University. All subjects were informed of any risks associated with participation in the study and signed an informed consent form prior to participation.

2.2.3 Exercise protocols

Immediately after the resting SBP and HR measures, the RE protocol began. Subjects started in a seated position, with their feet shoulder width apart, knees and hips flexed to 90 degrees, and their hands grabbing the handles set near the buttocks. On the examiner's command, the subject pushed the platform with both feet simultaneously until the legs were fully extended. Once full extension was reached, each person was instructed to immediately return to the starting position and to make sure that the weight plates encountered the stationary (unmoved) plates without slamming together. Subjects were verbally encouraged to perform the concentric phase of each repetition as fast as possible, to control the eccentric phase of each lift, and to finish all of the prescribed repetitions. Since water intake significantly decreases RPP for 20 min post ingestion (Monnard & Grasser, 2017), subjects were asked to avoid water intake of more than 355 ml 40 min before exercise. To avoid extreme blood pressures and according to common resistance training guidelines, subjects were asked to avoid performing a Valsalva maneuver by inhaling during the eccentric phase and exhaling during the concentric phase (Lamotte et al., 2010).

2.2.4 Statistical Analyses

Data were expressed as means $\pm$ SD. A Kolmogorov–Smirnov test was conducted to test

the normality of the data. A 2-way (protocol [2] × time [2]) repeated-measures ANOVA was used to compare RPP, SBP, and HR, with Tukey HSD Post Hoc test performed when necessary. Paired t-tests were used to compare the exercise time, RPP_{diff}, RPP_{perc}, SBP_{perc} (percentage of SBP change from pre- to post-exercise), and HR_{perc} (percentage of HR change from pre- to post-exercise) between protocols. Statistical significance was set at the $P<0.05$ level. The data were analyzed using JMP$^{@}$ pro 15 (SAS Institute Inc., Cary, NC, USA). A post hoc power analysis was 0.99 by using G*Power software (version 3.1.4), for the sample size of 14 with effect size of 1.54.

2.3 Results

All data were normally distributed, and every subject finished all of the prescribed repetitions. There was a significant difference in RPP between the protocols ($F_{1, 13}$ =18.13, P < 0.0009), as the RPP of single-set (17.48 ± 3.16 mm Hg · beat · min^{-1}) was significantly greater than that of multiple-set (13.66 ± 3.04 mm Hg · beat · min^{-1}). Also, post-exercise RPP (15.57 ± 3.85 mm Hg · beat · min^{-1}) was significantly greater than that of pre-exercise RPP (10.39 ± 2.09 mm Hg · beat · min^{-1}) ($F_{1, 13}$ = 67.62, P < 0.0001) in both exercise protocols. Further, there was a significant difference between exercise protocols and time effect on RPP ($F_{1, 13}$ = 45.36, P < 0.0001). Tukey HSD Post Hoc test found there was a significant difference between single-set and multiple-set post-RPP (t = 6.60, P < 0.0001), single-set post- and pre-RPP (t = 10.04, P < 0.0001), multiple-set post- and pre-RPP (t = 5.39, P < 0.0006), no significant difference between single-set pre- and multiple-set pre-RPP (t = 1.2, P > 0.64) (Figure 2.1).

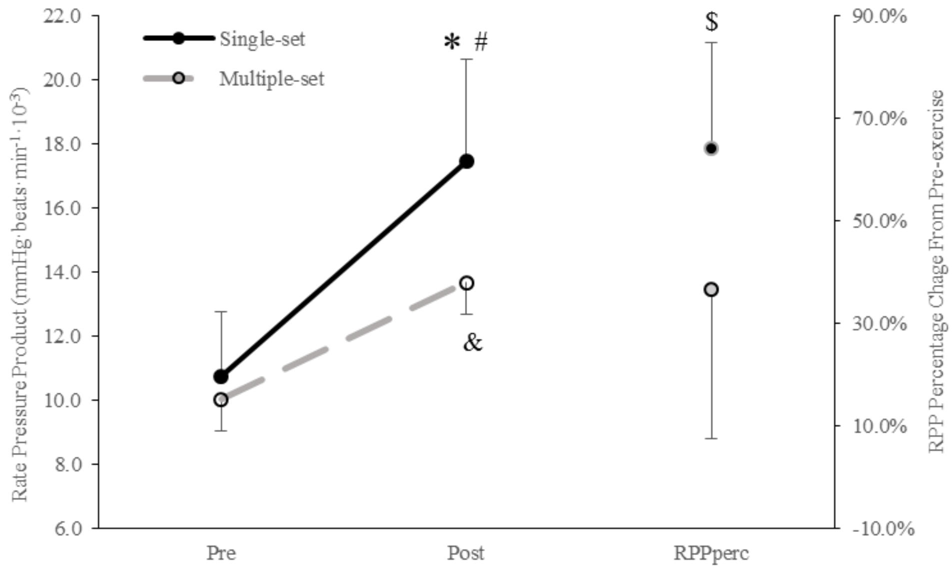

Figure 2.1. Pre and post-exercise RPP for single- and multiple-set exercises, percentage change of RPP for single- and multiple-set exercises (*, # P < 0.0001; & P < 0.0006; $ P < 0.0004).

There was no significant difference between exercise protocols ($F_{1, 13} = 2.61$, $P > 0.13$), protocol and time ($F_{1,1 3} = 2.52$, $P > 0.14$) effect on SBP, but post-SBP was significantly greater than pre-SBP ($F_{1, 13} = 54.66$, $P < 0.0001$) in both exercise protocols, Tukey HSD Post Hoc test found single-set post-SBP was significantly greater than pre-SBP ($t = 6.32$, $P < 0.0001$), Multiple-set post-SBP was significantly greater than pre-SBP ($t = 4.06$, $P < 0.007$) (Figure 2.2).

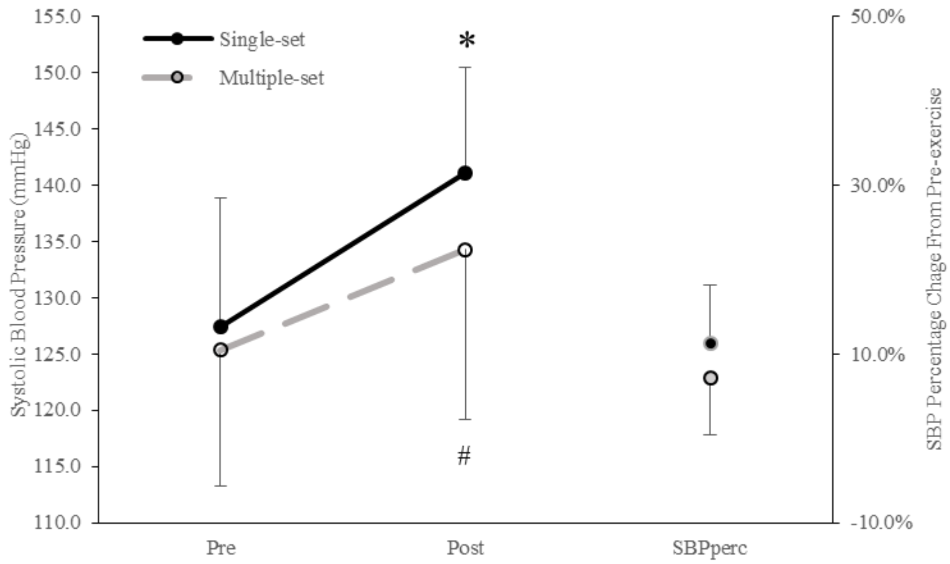

Figure 2.2. Pre and post-exercise SBP for single- and multiple-set exercises, percentage change of SBP for single- and multiple-set exercises (* $P < 0.0001$; # $P < 0.0065$).

There was a significant difference of exercise protocols ($F_{1, 13} = 18.66$, $P < 0.0008$), time ($F_{1, 13} = 56.89$, $P < 0.0001$), exercise protocols and time ($F_{1, 13} = 51.62$, $P < 0.0001$) effect on HR. Tukey HSD Post Hoc test found single-set post-HR was significantly greater than multiple-set post-HR ($t = 6.79$, $P < 0.0001$), single-set post-HR was significantly greater than pre-HR ($t = 9.36$, $P < 0.0001$), multiple-set post-HR was significantly greater than pre-HR ($t = 5.02$, $P < 0.001$), there was no significant difference between single-set pre- and multiple-set pre-HR ($t = 1.16$, $P > 0.67$) (Figure 2.3).

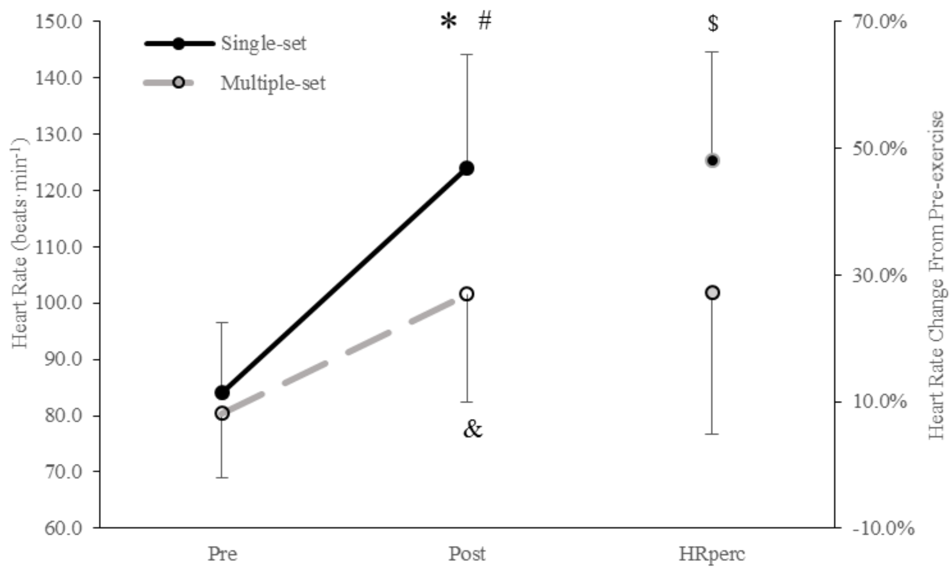

Figure 2.3. Pre and post-exercise HR for single- and multiple-set exercises, percentage change of HR for single- and multiple-set exercises (*, # P < 0.0001; & P < 0.0006; $ P < 0.0004).

The RPP_{diff} was significant difference in protocols ($t = 6.73$, $P < 0.0001$), the increased in single-set (6.74 ± 2.86 mm Hg · beat · min^{-1}) was greater than that of multiple-set exercise (3.62 ± 2.90 mm Hg · beat · min^{-1}) (Figure 2.4). RPP_{perc} of single-set was significantly greater than multiple-set ($t = 4.71$, $P < 0.0004$, See Figure 2.1), HR_{perc} of single-set showed the same effect as well ($t = 6.21$, $P < 0.0001$, Figure 2.3). There was no significant difference of SBP_{perc} for both exercise protocols ($t = 1.55$, $P > 0.15$, See Figure 2.2).

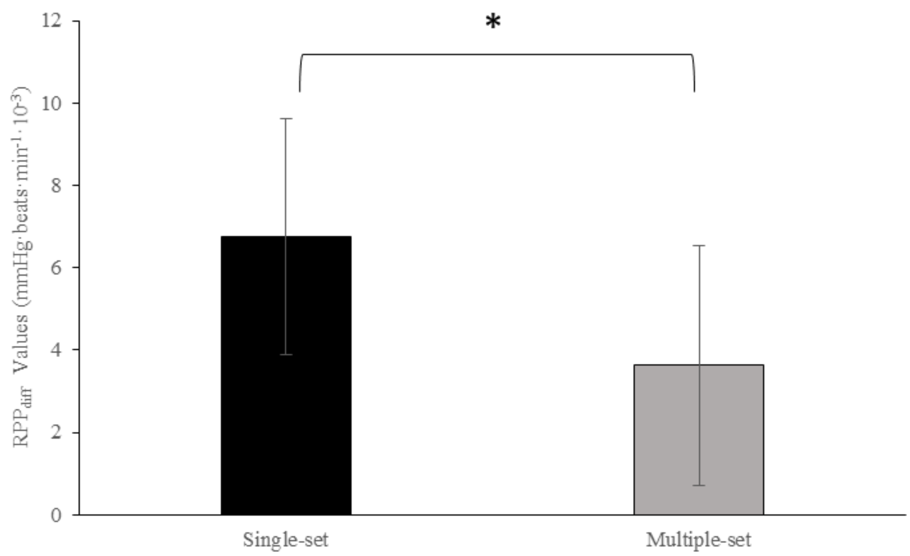

Figure 2.4. RPP_{diff} between two exercise protocols (* $P < 0.0001$).

The exercise time for single-set (84.21 ± 40.27 s) was 13.46 ± 38.35 s greater than that of multiple-set (70.76 ± 12.06 s), but no significant difference ($t = 1.31$, $P > 0.21$).

2.4 Discussion

The purpose of this study was to investigate the effect of volume-matched multiple- and single-set RE on the heart metabolism of untrained adults, through measuring RPP. Our main finding was that although the post-exercise RPPs were significantly greater than that of pre-exercise RPPs in both exercise protocols, post-exercise RPP was significantly greater for the single-set than for the multiple-set leg press protocol. Moreover, the RPP_{diff} and RPP_{perc} values were significantly greater in single-set than in multiple-set. However, HR and SBP, which are the factors of RPP, demonstrated different characters, only HR was significantly greater in single-set as compared to multiple-set. Interestingly, in contrast to previous study (Galvão & Taaffe, 2004) multiple-set is not superior to single-set in time efficient for finishing exercise.

Few studies have been conducted to examine the effect of volume-matched RE on cardiac stress, and the current study was the first to investigate the volume-matched single- and multiple-set RE on cardiac stress. In one study, trained subjects were asked to do parallel squats with the same volume load for either traditional training (3 sets to failure at 4 RM with 3 minutes rest between set), or cluster training (same volume load with rest time evenly separated between repetitions), which resulted in significantly greater RPP and SBP in traditional training than in cluster training (Iglesias-Soler et al., 2015). This was partially in agreement with the current study where RPP was significantly different between exercises, while instead of SBP, HR was significantly greater in single-set RE. Silva et al. (Silva et al., 2007) found SBP, HR and RPP were significantly greater in continuous protocol (no pause between repetitions) of bench press than that of two discontinuous protocols (pause 5 seconds or 10 seconds between the fifth and sixth repetitions). Though, these inconsistent results may have been due to differences in subject training status, exercise intensity, rest time, and study design, RPP should be a primary factor to be tested to investigate the effect of different RE on cardiac stress. Along with the aforementioned studies (Iglesias-Soler et al., 2015; Silva et al., 2007), the current study shows recovery time affecting RPP significantly, with the longer rest interval between repetitions or sets, the less increased in RPP. Thus, the single-set RE exerts a greater stress on cardiovascular system in comparison to multiple-set RE.

RE may have a negative effect on the vasculature by increasing vascular stiffness (Miyachi et al., 2004), which is associated with an augmented central pulse pressure (Pollock et al., 2000), an antecedent to the development of hypertension (Arnett et al., 2000). The current study is in agreement with previous studies (Iglesias-Soler et al., 2015; Polito et al., 2008; Río-Rodríguez et al., 2016; Silva et al., 2007) that volume-matched different type of REs

significantly increase RPP. A lower RPP for a given exercise task, suggests a reduced myocardial oxygen demand for that level of work (Fletcher et al., 2001). Thus, in the current study, multiple-set RE likely required less MVO_2 as compared to single-set. Additionally, Zapfe (Zapfe, 2001) concluded the lower RPP for a distinct work load, the more economical, in terms of oxygen utilization, it was for the heart muscle. In this regard, it is suggested that multiple-set RE is more efficient than single-set RE in terms of heart function. In clinical situations or cardiac rehabilitation programs, a peak RPP less than 36 mm Hg · beat · min^{-1} is considered safe (Jenny et al., 2008), and can range from 25 to 40 mm Hg · beat · min^{-1} for healthy individuals (Fletcher et al., 2001). In the current study, the RPP for single-set and multiple-set were 17.48 ± 3.16 and 13. 66 ± 3.04 mm Hg ·beat · min^{-1} respectively, far less than the abovementioned values. One of the reasons could be ascribed to the RPP of RE is significantly lower as compared to aerobic exercise (Jenny et al., 2008). The subjects in the current study were untrained adults, who experienced a higher pressor response to resistance exercise as compared to resistance trained participants (Fleck & Dean, 1987). However, due to the values of RPP being significantly lower than that would trigger angina pain (23 mm Hg · beat · min^{-1}) (Robinson, 1967), it could be suggested that both multiple- and single-set REs in the current study are safe for untrained adults.

In the current study, post-exercise SBP and HR significantly increased in both exercise protocols, which is in agreement with previous volume-matched studies (Polito et al., 2008; Silva et al., 2007). However, the increased SBP in the current study contradicted other studies that claimed RE had a hypotensive effect on the heart (de Freitas Brito et al., 2014; Rezk et al., 2006). The potential reason could contribute to muscle fatigue, because the current exercise protocols consisted of high intensity, high-volume RE, with 40 repetitions at 150% body weight of each exercise. As the muscle approaches fatigue, more relative effort is required, accessory

muscles may be recruited, and muscle nociceptors may be stimulated, which may contribute to elevating the SBP (Gotshall et al., 2001). This could also explain the non-significant exercise time between two exercise protocols, subjects were fatigue faster in single-set with 40 repetitions protocol, thus tended to finish the prescribed exercise slower than expected. On the other hand, the HR was significantly greater in single-set than that of multiple-set, which contributed to the RPP difference between two exercise protocols. The result was contrary to the previous statement that SBP that may contribute more than HR to the increase in RPP during resistance exercise (Graves & Franklin, 2001). Goldstein and Epstein (Goldstein & Epstein, 1973) explained that a given increase in the RPP might have different implications depending on whether that increase was due to a rise in HR, or a rise in SBP. Thus, the observation of HR or BP alone does not guarantee client safety (Simonson & Wyatt, 2003). This is in accordance with our previous statement that RPP should be used to monitor RE on cardiac stress.

RPP reserve (maximal exercise RPP minus resting RPP) has greater prognostic power than metabolic equivalents, maximal HR or systolic blood pressure, or HR recovery, with a lower RPP reserve yielding a higher mortality (Rafie et al., 2008). Moreover, Saunamäki and Andersen (Saunamäki & Andersen, 1981) found that the probability of survival was significantly worse in patients with a low RPP reserve than those with a high RPP reserve, and found the discriminating values of RPP reserve for myocardial infarction (MI) was between 1.5 and 2.5 mm Hg · beat · min^{-1}. In the current study, the RPP difference as compare to resting was 6.74 ± 2.86 and 3.62 ± 2.90 mm Hg · beat · min^{-1} for single-set and multiple-set RE respectively, both of which were greater than the discriminating values of Saunamäki and Andersen (Saunamäki & Andersen, 1981). Our results, however, should not be related to work done in a clinical setting. The current study measured healthy subjects, and the RPP were not obtained from maximal

exercise. Thus, in order to examine the RPP reserve of RE on the predicting of heart disease, more studies are needed. Taken altogether, the difference of RPP in both exercise protocols in current study demonstrated single-set RE puts a significant greater stress on the heart as compared to multiple-set RE.

Single- and multiple-set REs have been a debatable topic for the past decades for their physiological effects on human body. One of potential benefits of single-set RE to many individuals is the accomplishment of similar outcomes with less time. A study showed only 15 min of a single-set bout of RE was as effective as a three-set protocol of 35 min in elevating resting energy expenditure (REE) for up to 72 hours (Heden et al., 2011). Moreover, a single-set program resulted in similar strength gains as multiple-set program in untrained individuals (Wolfe et al., 2004). Galvao and Taaffe (Galvao & Taaffe, 2005) concluded that single-set exercise was sufficient to significantly enhance muscle function and physical performance. These findings lead to design time-efficient exercise regimens to enhance neuromuscular function in humans. On the other hand, Kemmler, Lauber, Engelke, and Weineck (Kemmler et al., 2004) suggested multiple-set protocols were superior to single-set protocols in increasing maximum strength in postmenopausal women. Krieger (Krieger, 2010) stated in a meta-analysis study that multiple-set was associated with 40% greater hypertrophy-related effect sizes than single-set, in both trained and untrained subjects. Furthermore, McBride, Blaak, and Triplett-McBride (McBride et al., 2003) suggested that multiple-set or a greater volume of RE produced optimal gains in strength even for relatively untrained persons, especially in simple exercise movements. Therefore, considering the abovementioned research, single-set and multiple-set RE affect the human body in different ways. However, when taking into account of the effect on cardiovascular system, single-set RE exerts more stress on the heart. From a training and clinical

perspective, single-set RE appears preferable for training the heart, while multiple-set would appear best for those who should avoid heart stress, such as people with heart diseases, post-cardiac surgery patients and senior populations.

There were some limitations for this study: Firstly, the BP was measured indirectly by an auscultatory method. One study argued that auscultation can underestimate the intra-arterial value and suggested intra-arterial catheterization of BP to be used (Holland & Humerfelt, 1964), and the mean overall SBP measured by catheter was 29.0 mm Hg greater than BP measured by cuff (Rasmussen et al., 1985). Nevertheless, the two methods have a very high degree of correlation (coefficient of correlation = 0.95 for SBP) (Holland & Humerfelt, 1964). Therefore, the auscultatory method could be considered an appropriate method to compare training conditions because a high correlation between direct and indirect methods (Sagiv et al., 1995). Secondly, high volume load was used, especially for single-set RE. It was not a practical RE protocol and fatigue may show early, thus impairing the training effect. Finally, only untrained individuals were recruited, and if strength trained subjected were involved, the results may have been different.

In conclusion, HR and SBP reacted differently in response to the current exercise protocols. In order to fully understand the RE on cardiac stress, RPP should be a primary targeted factor. In the current study, a single-set of RE exerts more metabolic stress on the cardiovascular system than doing the same workload of multiple-set RE. Thus, single-set RE could be used for training cardiac tissue. On the other hand, multiple-set RE is recommended for people with compromised cardiovascular systems. From a training and clinical perspective, multiple-set RE would appear best for those who should avoid heart stress, such as people with

heart diseases, post-cardiac surgery patients and senior populations, while single-set appears preferable for training the heart.

CHAPTER 3. MUSCLE SENTRY® HAS NO EFFECT ON TOTAL WORK PERFORMED AND ESTIMATED MVO_2 AFTER HIGH INTENSITY SHORT DURATION RESISTANCE TRAINING

3.1 Introduction

Our laboratory recently published a study that determined if Muscle Sentry® (Muscle Sentry LLS, Cleveland, OH) would increase muscle stamina (i.e. endurance) on both the basis of a single task and a repeated task (Bartschi et al., 2017). The main finding from that investigation was that the number of lifts did not differ between the Muscle Sentry® and placebo treatments for either the initial or the repeated sets. Thus, it appeared that the Muscle Sentry® had no influence upon stamina when doing a task designed to fatigue a muscle after 2 minutes of work.

In retrospect, since some of the ingredients (Table 1.) found in this supplement have shown positive effects in work of short duration and higher intensity, it is still possible that this supplement will have an effect if used in different work scenarios. Muscle Sentry® purported benefits upon stamina arise from ingredients that include various minerals complexed with lactate and red cinchona bark powder, a source of quinine. Morris (Morris, 2012) has pointed out that exogenous lactate could be used as an energy substrate and as a buffering agent. Moreover, ingestion has been shown to increase blood pH, bicarbonate levels and increase time to exhaustion in short, high-intensity work bouts. On the other hand, Muscle Sentry® is unique in that it contains red cinchona bark powder, a source of quinine. Gam et al. (Gam et al., 2014) have shown that ingesting a 2mM solution of quinine improved the mean power output during a 30 s cycling sprint.

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Given that the ingredients found in Muscle Sentry® have been found to be beneficial in intense work bouts lasting ≤30 seconds, it is quite possible that the negative findings of our original study were due to the work lasting two minutes or 2.5 times longer than previous studies that showed positive effects. Therefore, the purpose of this study was to investigate the effects of Muscle Sentry® upon the amount of total lift numbers on repeated high-intensity short duration work. In addition, since Muscle Sentry® manufacturer's claim that using this supplement leads to increased cardiovascular efficiency, we also investigated the supplement's effect upon myocardial work. In this context, we hypothesized that intake of Muscle Sentry® would increase total muscle lift numbers and estimated MVO_2.

Table 3.1. Muscle Sentry® active ingredients.

Supplement	Serving Amount
Niacin	50 mg
Pyridoxine HCL (vitamin B6)	9 mg
Calcium Lactate	32.5 mg
Magnesium Lactate	50 mg
Zinc Oxide	25 mg
Manganese Lactate	16 mg
Potassium Chloride	50 mg
Red Cinchona Bark Powder	600 mg

3.2 Methods

3.2.1 Participants

Participants consisted of 11 female (age = 21 ± 1 y, height = 161 ± 8 cm, body mass = 61 ± 9 kg; mean ± standard deviation) and 10 male (age = 22 ± 1 y, height = 180 ± 4 cm, body mass = 73 ± 28 kg; mean ± standard deviation) physical education college students. Inclusion criteria: non-resistance trained, healthy, normotension (< 120/80 mm Hg), no supplements or medication intake for more than one year. Exclusion criteria: pre-hypertension (between 120/80 mm Hg and 139/89 mm Hg), hypertension (> 140/90 mm Hg), cardiovascular disease and/or obesity (BMI >

30.0). This research was carried out fully in accordance to the ethical standards of the International Journal of Exercise Science (Navalta et al., 2019). Informed consent (written and verbal) was obtained from each participant before commencing the experiment, and the appropriate institutional human participant review committee approved the study. The participants were not allowed to see the results until the study was completed. The number of participants needed for a statistical power of $\beta = 0.20$ was determined using an online calculation website (www.sample-size.net).

3.2.2 Study Design

Participants visited a weight room 5 times on different days separated by a minimum washout of seven days. On all experimental testing days, each participant performed 3 sets to failure on both a seated chest press and a leg press machine. The first experimental day consisted of the participants performing the chest and leg presses to determine their 8 repetitions maximum (8RM) weight. Days 2-5 consisted of doing 3 sets to failure with the 8RM weight for both chest and leg presses. An 8 RM was chosen because a common resistance training program consists of doing 3 sets of 8-10 reps. In a randomized counter-balanced manner, for two days the lifts were performed on Muscle Sentry®, while for the other two days were performed on a placebo. The dose for Muscle Sentry® was based upon body mass (i.e. 1 capsule for body weights < 160 lbs.; 2 capsules for body weights between 160 lbs. and 240lbs.; and 3 capsules for body weights > 240 lbs.). The placebo (powdered cellulose) consisted of the same amount of pills and these pills were similar in shape and color to Muscle Sentry®. In addition to count the total number of lifts, heart rate and blood pressure were measured at the beginning and end of each set to failure.

3.2.3 Muscle 8RM and Stamina Test Protocol

As stated, the first experimental testing day consisted of each participant performing an 8RM on the chest press and leg press machine. The chest press was performed seated on a Body Masters vertical chest press machine (Body Masters Sports Industries Inc., Rayne, LA, USA). The initial weight was set at 75% of body mass. After performing 8 lifts at this weight, the participant rested for two minutes with the next lift increased incrementally by multiples of 44 N (10 lbs.). Following a 2- minute rest, each succeeding 8 repetitions set was incremented by 44 N (10 lbs.) until failure to complete 8 repetitions. For all repetitions, participants were instructed to push upward until they reached full elbow extension as quickly as possible. Once full extension was reached, each person was instructed to return as quickly as possible to the starting position while making sure that the weight plates contacted the stationary (unmoved) plates.

The leg press was performed in a seated position using a Body Masters leg press machine (Body Masters Sports Industries Inc., Rayne, LA, USA). Prior to beginning the test, participants were seated in the apparatus with the seat position being adjusted so that the individuals starting knee angle approximated 60^{o}. The participants were instructed to push on the footplate until they reached full knee extension as quickly as possible. Once full extension was reached, it was instructed to return as quickly as possible to the starting position while making sure that the weight plates contacted the stationary (unmoved) plates. The initial weight was set at 150% of body mass, and the procedure was the same as that used for the chest press. The only difference was that the ensuing 8 repetitions set was increased incrementally by multiples of 66 N (15 lbs.) after each 2-minute rest.

For the subsequent 4 experimental testing days (day 2-5), participants reported to the laboratory 2 hours post-prandial and were instructed to consume either the Muscle Sentry® or

placebo supplement. Following supplement consumption, all participants rested quietly in the laboratory for 40 minutes. Once the rest period was completed and depending upon which lift was scheduled to be first, participants began a standardized warm-up by performing 8-reps at 50% of their 8RM on either the chest press or leg press. Right after warmup, each participant performed 3 sets to failure using 8RM, with two minutes rest between sets. Upon completion of the 3-set lift, a 5-minute rest was taken. Once the 5 minutes rest was completed, participants performed a secondary warm-up of 8 reps at 50% of 8RM on the opposite lift from which they performed first. The same procedure was proceeded for the succeeding press. To ensure that all lifts were performed correctly and without too much rest, two members of the experimental team watched the subject to ensure their joints were full extended and then the weight plates returned to the starting position. These two investigators also ensured that each extension and flexion were done without any rest at either full extension or at weight plate touch. A third individual who was unaware of the supplement taken that day counted the number of lifts. Failure was set at the lift at which the person could not reach full (elbow or knee) extension.

Besides improving stamina, the manufacturer claims that the supplement improves cardiovascular efficiency. To test this, it was decided to compare the post-exercise rate pressure product (the product of heart rate and systolic blood pressure). The rate pressure product (RPP) has been shown to be a reliable and meaningful predictor of myocardial oxygen consumption (MVO_2) during static and dynamic exercise (Nelson et al., 1974). Therefore, heart rate (HR) and blood pressure (BP) were obtained just prior to commencing and immediately after each set to failure. HR and BP were measured using an automated device (Omron BP710, Omron Healthcare Inc., Bannockburn, IL, USA) which had previously been shown to provide reliable and accurate values (Nelson et al., 2015). Since HR and BP vary with work volume, for analysis

the post-RPPs were normalized by dividing the RPP by the total weight lifted in each respective lift.

3.2.4 Statistical Analysis

For each treatment, subject performed twice with chest press and leg press exercises. In order to reduce the variability between the exercise performance, an average parameter for each treatment was calculated, including average number for chest lift , leg lift, and total lift, average values for normalized post RPP (NPRPP), and normalized pre and post exercise rate pressure product difference (NRPPdiff). A one-way ANOVA was used to compare the treatments effect on each of the aforementioned variables. A two-way (gender × treatment) ANOVA was used to test the treatment effect on lift numbers by gender. A two-way (gender × RPP) ANOVA was used to test treatment effect on $NRPP_{diff}$, NRPP in gender. Tukey test was used for the Post Hoc analysis, for any significant differences. Statistical significance was set at alpha level as 0.05. All analyses were conducted by using SAS software (SAS 9.4, SAS Institute Inc., NC, USA).

3.3 Results

The average chest lift, average leg lift and average total lift numbers for both treatments are depicted in Figure 3.1. There were no significant differences for treatment effect on chest lift ($p = 0.94$), leg lift ($p = 0.86$) and whole body lift numbers ($p = 0.87$). In addition, there was no significant difference ($p > 0.05$) between the number of repetitions (lifts) for both within and between treatment days for each set (i.e. set 1, set 2, and set 3 had a statistically similar number of lifts in all instances).

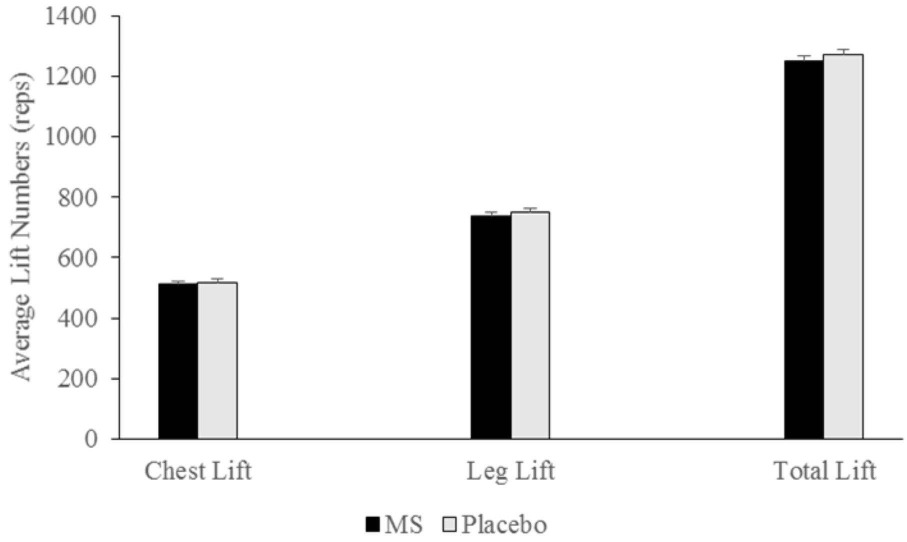

Figure 3.1. Average Lift Numbers between treatments (MS: Muscle Sentry®).

There was no significant difference in treatment effect on gender, for average chest lift numbers ($p=0.87$), average leg lift numbers ($p=0.95$), and average total lift numbers ($p=0.96$) (Figure 3.2).

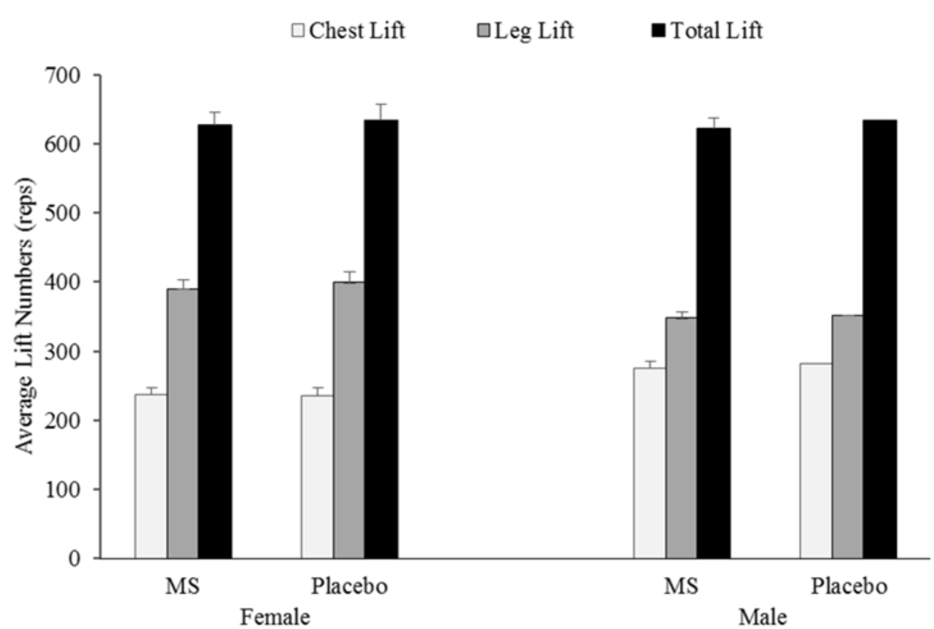

Figure 3.2. Treatment on different lift numbers for gender (MS: Muscle Sentry®).

Finally, there was no significant difference between the treatments on either $NRPP_{diff}$ or NPRPP ($p = 0.43$, 0.87 respectively) (Figure 3.3). There was, however, a significant difference between gender on NPRPP ($F = 35.22$, $p < 0.001$), independent of treatments. Furthermore, there was a significant difference between gender on $NRPP_{diff}$ ($F = 7.77$, $p < 0.008$) (Figure 3.4), meaning post RPP increased more in females than that in males.

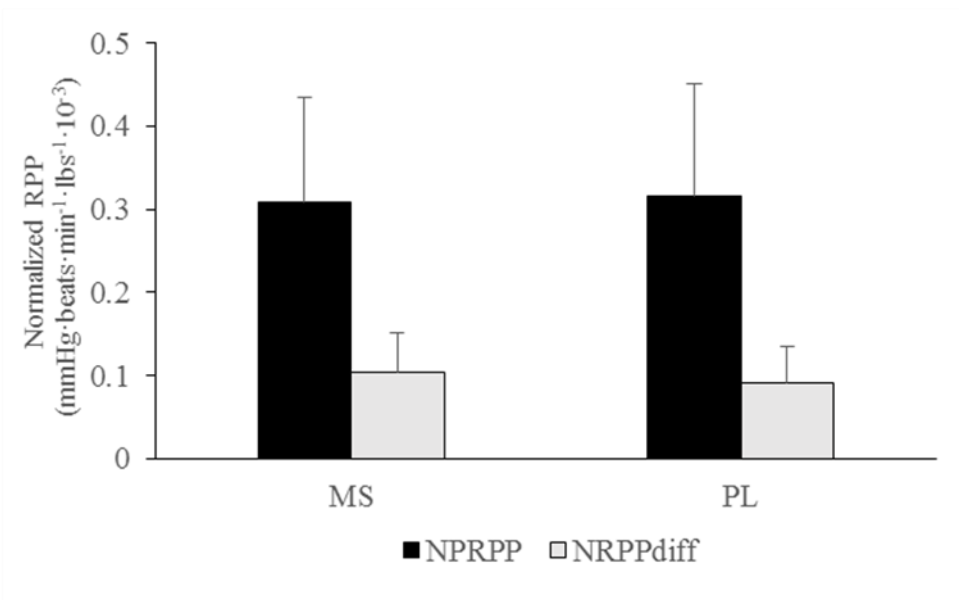

Figure 3.3. NPRPP and $NRPP_{diff}$ for Muscle Sentry and Placebo (MS: Muscle Sentry®; PL: Placebo).

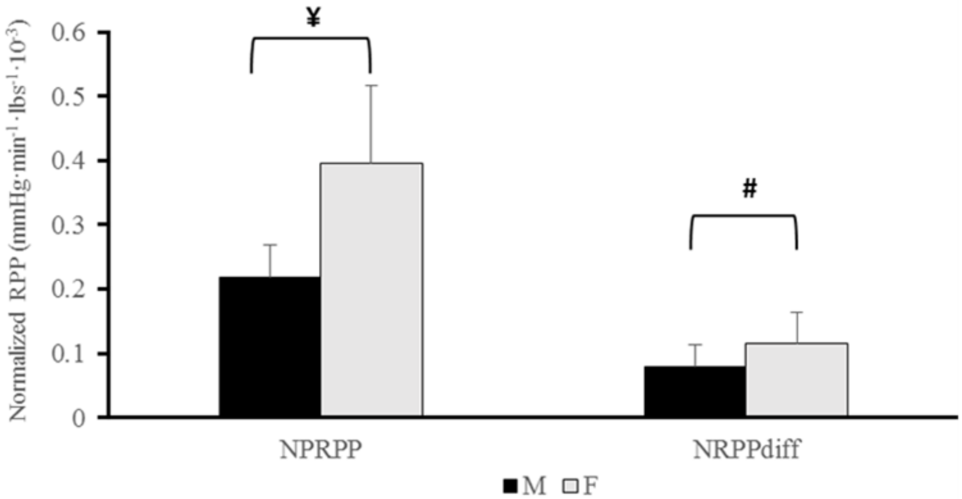

Figure 3.4. NPRPP and $NRPP_{diff}$ for Gender (M: male, F: female; ¥, # P<0.05).

3.4 Discussion

The goal of this study was to determine if ingestion of Muscle Sentry® would increase the amount of lift numbers on repeated high-intensity short duration exercise. The main finding was that Muscle Sentry® did not have any statistically significant effects on the magnitude of high-intensity work performance for an exercise program using chest press and leg press machines. Additionally, Muscle Sentry® did not result in improving myocardial work capacity. Taken together with our lab's previous study (Bartschi et al., 2017) of a lack of an increase in muscle stamina with Muscle Sentry®, we can conclude again that Muscle Sentry® does not have any effect on muscle work or myocardial work performance when performing resistance exercise at either a moderate-intensity, long-duration bout, or high-intensity, short-duration bout.

High-intensity, short-duration exercise requires maximal or near-maximal intensity efforts resulting in rapid changes in the intramuscular metabolic profile (Junior et al., 2015), as of which these changes are accompanied by muscle fatigue (Fitts, 1994). Scholars have demonstrated that high-intensity, short-duration exercise induced fatigue can be contributed to an

accumulation of potassium ions (K^+) in the interstitium of the muscle cell (Sejersted & Sjøgaard, 2000), decreased release/uptake of calcium ions (Ca^{2+}) from/to the sarcoplasmic reticulum (Hirano et al., 2000), depletion of energy substrates, and the accumulation of metabolites within the muscle cell (Robergs et al., 2004). Junior and his colleagues (Junior et al., 2015) have demonstrated that muscle pH homeostasis is mainly regulated by intracellular, extracellular, and dynamic buffering system during high-intensity, short-duration exercise (Junior et al., 2015). Lactate supplementation has been suggested to increase extracellular buffering capacity (Van Montfoort et al., 2004), but studies related its effect to exercise performance during high-intensity exercise are controversial. For example, Van Montfoort et al. (Van Montfoort et al., 2004) reported participants' exercise capacity improved by 1.7%, following a run to exhaustion supplemented with a dose of 400 mg · kg^{-1} body mass (BM) of sodium lactate. Furthermore, Morris et al. (Morris et al., 2011) found that supramaximal multiple bout cycling time to exhaustion and total work increased by 17% when the cyclists were supplemented with 120 mg · kg^{-1} BM calcium lactate. However, Painelli and his colleagues (Painelli et al., 2014) reported that neither 150 mg · kg^{-1} BM nor 300 mg · kg^{-1} BM of calcium lactate improved high- intensity intermittent performance in the form of three upper-body arm-crank bouts. One potential explanation for the inconsistence in findings could be related to the individual exercise protocols (Junior et al., 2015). Furthermore, the aforementioned investigations administrated similar high-dose, therefore, providing doubt and further controversy on the efficacy of lactate supplementation (Junior et al., 2015). On the other hand, the dose recommended by Muscle Sentry® and used in current study, was much less than the amount consumed in the aforementioned studies. Therefore, it is reasonable to conclude that Muscle Sentry® would not increase performance of high-intensity, short-duration exercise.

Red cinchona bark is a source of quinine that has been used since the early 1600s to treat malaria (Achan et al., 2011). However, the therapeutic function of quinine is equivocal. On one side, quinine is a cinchona alkaloid that belongs to the aryl amino alcohol group of drugs (Hellgren et al., 2014), with alkaloid being known to stimulate cardiovascular and neurological function resulting in decreased sensations of fatigue during physical stress (Robergs et al., 2003). Thus, quinine has the potential to improve exercise performance. Unfortunately, quinine has a low therapeutic index with adverse effects with its use being substantial (Organization, 1990). One common side effect is hypoglycaemia (plasma glucose concentration < 2.8 mmol · L^{-1}), and occurs in up to 32% of patients receiving quinine therapy (Okitolonda et al., 1987). There are scant studies relating the ergogenic effect of quinine on exercise performance, and those results are inconsistence. For example, Gam et al. (Gam et al., 2014) found that a combination of mouth rinsing and ingestion of a 2 mmol · L^{-1} bitter quinine solution immediately before a maximal 30s cycling sprint improved mean and peak power output. In another study, Gam and colleagues (Gam, Guelfi, et al., 2015) found that motor-evoked potentials (MEPs) were significantly increased by 16% immediately after mouth rinsing and ingestion with the same 2 mmol · L^{-1} quinine solution. They further suggested that the increased MEPs were the cause of the improvement of maximal cycling sprint performance. The conclusions of the above studies were based on the theory that a bitter solution may activate emotional and motor areas of the brain, as well as the autonomic nervous system, all of which might have impacted the maximal sprint performance (Gam et al., 2016). However, since Muscle Sentry® is an encapsulated supplement, it cannot have a similar ergogenic effect as the supplements used in aforementioned studies. On the other hand, Gam et al. (Gam, Tan, et al., 2015) did not find the improvement of 30s cycling sprinting performance, when rinsing mouth only with higher concentration 10 mmol · L^{-1} of

quinine solution. Moreover, in contrast to the findings of enhanced MEPs (Gam et al., 2014; Gam, Guelfi, et al., 2015), Fung and Holbrook (Fung & Holbrook, 1989) noted that quinine administration showed a decrease in the excitability of the motor end-plate region resulting in a reduced response to repetitive nerve stimulation. Additionally, there are no studies supporting the manufacturer's claim that quinine could be an enabler to improve the performance of other supplements (Hadala & Bennett, 2013). Hence, it is reasonable to conclude that Muscle Sentry® has no significant effects on high-intensity short duration resistance exercise.

The current study did not find any significant effect of Muscle Sentry® on cardiovascular efficiency, which contrasted Peacock et al. (Peacock et al., 2012) who reported a significant mean increase of 3 $ml \cdot kg^{-1} \cdot min^{-1}$ in VO_{2max} following ingestion of Muscle Sentry®. However, VO_{2max} and MVO_2 do not necessarily change in parallel with various exercises (Nelson et al., 1974). Thus, one cannot simply conclude any improvement in VO_{2max} due to ingestion of Muscle Sentry® will increase cardiovascular efficiency. Interestingly, the current study showed women had higher amount of NPRPP and $NRPP_{diff}$ ($p = 0.001$, 0.008 respectively) than that of men independent of treatments. This suggests that the women experienced more cardiac stress after the high-intensity short duration resistance exercises. The current finding supports a previous study that the female's response to upper extremities isometric exercise was higher than that of the males (i.e. the women had higher RPPs) (Mbada et al., 2009). However, since the exercise protocol was different in these studies (concentric vs. isometric); it is possible that the mechanisms would also be varied.

Finally, it should be noted that the study was designed to investigate the effect of Muscle Sentry® on muscle stamina of untrained people. Since its effect on trained individuals was not examined, Muscle Sentry® may have a significant different effect upon these two populations.

We hypothesized, however, that the benefits of Muscle Sentry® would be better explored by using people who could benefit the most from enhanced stamina, i.e. the untrained or individuals at the lower-end of the stamina continuum. Another limitation of this study was only two exercises were utilized; a number less than normal seen in a regular resistance exercise training (i.e. 5-10 lifts in most cases). Therefore, further studies are needed to examine the effect of Muscle Sentry® on trained people with multiple sets and more resistance exercises. Ingestion of Muscle Sentry® did not increase exercise performance or heart function during high-intensity short duration resistance exercise.

CHAPTER 4. ACUTE EFFECT OF N-ACETYLCYSTEINE ON CARDIOVASCULAR RESPONSES TO REGULAR CONVENTIONAL RESISTANCE EXERCISE

4.1 Introduction

N-acetylcysteine (NAC) is a sulfhydryl-containing antioxidant used clinically as an acute antidote to acetaminophen overdose and as a pulmonary mucolytic agent (Flanagan & Meredith, 1991). Emerging data, however, have shown NAC intake inhibits fatigue after repeated bouts of intermittent exercise (Cobley et al., 2011), handgrip exercise (Matuszczak et al., 2005), and improves quadriceps endurance in patients with COPD (Koechlin et al., 2004). Moreover, studies also showed NAC intake optimizes heart function. NAC improves human coronary and peripheral endothelium dependent vasodilation (Andrews et al., 2001). Evidence also showed NAC administration to improve ejection fraction without affecting blood pressure in Syrian Cardiomyopathic Hamsters (Crespo et al., 2011). It is well known that MVO_2 depends on myocardial oxygen supply and demand (Tousoulis, 2017). The supply of oxygen to the myocardium is determined by the oxygen-carrying capacity of the blood and the magnitude of coronary blood flow (Ardehali & Ports, 1990). Thus, in this context, NAC intake may reduce exercise MVO_2, leading to the decrease of heart stress.

Although conventional resistance exercise (RE) has been recognized as one of treatments for cardiovascular diseases (Williams et al., 2007), central arterial compliance in young and middle-aged resistance trained men is decreased compared with sedentary age matched controls (Bertovic et al., 1999; Ling et al., 1995). Decreases in the elastic properties of the arteries reduce the buffering capacity of the arteries, leading to increased pulse pressure, aortic impedance, and left ventricular wall tension (O'Rourke, 1990; Tanaka et al., 1998), all of which augment the

workload of the heart (DeVan et al., 2005). Therefore, RE can have a negative effect on the heart.

In the light of the benefits mentioned above on the heart, administration of NAC during RE may reduce the stress pressor that RE exerts on the heart. Rate pressure product (RPP) is an indicator of myocardial oxygen uptake and coronary blood flow in the exercise test (Fletcher et al., 2001), and a good measure of MVO_2 (Medicine, 2006), thus was used to as a measurement of MVO_2 in the current study. Previous studies found acute RE increased RPP (Maior et al., 2014b; Nogueira et al., 2007), however, these results were based on either a single set of RE or a simple RE workout that is not regularly performed. Therefore, in the current study, 6 regular conventional REs were performed with NAC to examine the adaptation of RPP. The purpose of this study was to investigate the effect of NAC intake with conventional RE on the heart, through examining RPP. We hypothesized that regular conventional RE would increase RPP, and NAC intake would lower RPP as compared to placebo.

4.2 Methods

4.2.1 Study design

The experiment was a randomly assigned, double-blinded, crossover design in which all subjects submitted to two experimental trials: a placebo (Psyllium fiber: PLA) or experimental (N-acetylcysteine: NAC) trial at a dosage of 1800 mg (3 × 600 mg). Subjects came to lab for a total 5 times including 1) a familiarization trial for all 6 exercises, including leg extension (LE), seated chest press (SCP), leg curl (LC), seated row (SR), seated shoulder press (SSP), and lat pull-down (LPD), 2) a strength fitness testing trial, 3) a 1RM test trial, and 4) & 5) treatment trials. Each trial was conducted on the same time of the day for each subject, and the interval between sessions was at least 48 hours for trials 1-3 and one week for trials 4 & 5. During the

experimental trials, supplements were taken 1 hour before exercise, rest HR and SBP were measured after 10 min seated rest in the lab, post-exercise HR and SBP were taken immediately at the end of each set of exercise always using the same procedure. All evaluations were executed by the same experience researcher, and were conducted on the subject's left arm with seated position. RPP was calculated as HR × SBP × 10^{-3} mm Hg · beats · min^{-1}.

4.2.2 Participants

Twelve college students participated in this study, three were not included in data analysis: one participant's rest SBP was greater than 158/90 mm Hg, and two other participants did not finish the trial due to COVID-19 pandemic. Therefore, total 9 participants (7 females, 2 males; Age: 20.25 ± 0.87 y; Height: 1.67 ± 0.10 cm; Weight: 67.87 ± 9.48 kg) finished the study. Inclusion criteria consisted of: college student who currently engaged in a minimum of 30 minutes of resistance exercise twice a week, healthy, normotension (< 120/80 mm Hg), good strength fitness, no nutraceuticals or medication intake for more than one year, and no supplementations of any kind throughout testing. Exclusion criteria consisted of: pre-hypertension (between 120/80 mm Hg and 139/89 mm Hg), hypertension (> 140/90 mm Hg), cardiovascular disease and/or obesity (BMI > 30.0). Each subject was required to fill out the Physical Activity Readiness Questionnaire (PAR-Q) (Shephard, 1988), and any subject who answered one of the questions with "yes", was excluded from the study. Coffee, tea, alcohol, tobacco intake, or any other substance that is known to affect HR or BP was prohibited for 48 hours prior to testing as well as avoidance of any formal and strenuous exercise. This study was approved by the Institutional Review Board (IRB) of the Louisiana State University. All subjects were informed of any risks associated with participation in the study and signed an informed consent form prior to participation.

4.2.3 Strength fitness test

In order to assure subjects had similar training levels, each subject's strength fitness was tested by the method described elsewhere (Hoeger & Hoeger, 1992). Briefly it went as follows: subjects were asked to perform six exercises: lat pull-down, leg extension, bench press, sit-up, leg curl, and arm curl, doing as many repetitions as possible at a resistance corresponding to their body weights (Table 4.1), the percentile rank of each lift was obtained according to the repetitions performed (Table 4.2), finally, an overall strength fitness level was determined by an average percentile score for all six exercises (Table 4.3). The average score of fitness level for all subjects was excellent (89.64).

Table 4.1. Resistance Lifting Table

Lift	Percent of Body Weight	
	Men	Women
Lat Pull-Down	0.70	0.45
Leg Extension	0.65	0.50
Bench Press	0.75	0.45
Sit-Up	0.16	0.10
Leg Curl	0.32	0.25
Arm Curl	0.35	0.18

Note. Reprinted from Lifetime Physical Fitness and Wellness (3rd ed., p 57), by W. WK. Hoeger, S. A. Hoeger, 1992, Morton Publishing Company. Copyright 1986, 1989, 1992 by Morton Publishing Company.

Table 4.2. Muscle Strength and Endurance Scoring Table

MEN						
Percentile Rank	Lat Pull-Down	Leg Extension	Bench Press	Sit-Up	Leg Curl	Arm Curl
99	30	25	26	30	24	25
90	19	19	19	23	19	19
80	16	15	16	17	15	15
60	11	13	11	12	11	10
40	9	10	7	8	8	8
30	7	9	5	5	6	7

Table cont'd

WOMEN						
Percentile Rank	Lat Pull-Down	Leg Extension	Bench Press	Sit-Up	Leg Curl	Arm Curl
99	30	25	27	32	20	25
90	21	18	20	22	12	20
80	16	13	16	14	10	16
60	11	10	11	6	7	12
40	9	8	5	4	5	8
30	7	7	3	2	4	7

Table cont'd

Note. Adapted from Lifetime Physical Fitness and Wellness (3rd ed., p 58), by W. WK. Hoeger, S. A. Hoeger, 1992, Morton Publishing Company. Copyright 1986, 1989, 1992 by Morton Publishing Company.

Table 4.3. Muscle Strength Category

Average Score	Endurance Classification
≥81	Excellent
61-80	Good
41-60	Average
21-40	Fair
≤20	Poor

Note. Reprinted from Lifetime Physical Fitness and Wellness (3rd ed., p 57), by W. WK. Hoeger, S. A. Hoeger, 1992, Morton Publishing Company. Copyright 1986, 1989, 1992 by Morton Publishing Company.

4.2.4 One Repetition Maximum Testing (1RM)

The 1RM testing protocol (Brown & Weir, 2001) was used. After resting HR and SBP were measured, the subjects performed a specific warm-up set of 8 repetitions at approximately 50% of the estimated 1RM followed by another set of 3 repetitions at 70% of the estimated 1RM. Subsequent lifts were single repetitions of progressively heavier weights until failure. Failure was considered when a participant could not complete a repetition (i.e. muscular failure), by not reaching the target position for two successive repetitions (i.e. technical failure) (Iglesias-Soler et al., 2015). Each subject had a maximum of five 1RM attempts of each exercise with 1 minute rest between attempts (Pichon et al., 1996). The testing order was LE, SCP, LC, SR, SSP, and LPD, and rest interval between each 1 RM test was no shorter than 5 minutes. To minimize

possible errors in the 1RM tests, all subjects received standard instructions of exercise technique of each exercise before testing, and received verbal encouragement during testing. Post-exercise HR and SBP were measured immediately after the last attempt of 1RM test for each exercise.

4.2.5 Exercise Protocol

Traditional weight training programs involve lifting a weight of about 60% to 80% 1RM, with 2-3 sets of 8 to 10 reps for each exercise, and resting for 1 to 2 min between sets (Pichon et al., 1996). Therefore, we formulated a conventional RE program, including LE, SCP, LC, SR, SSP, and LPD. Initially, subjects were randomly assigned to receive either the supplement or placebo, and then were assigned to the remaining treatment after a 1-wk washout period following the completion of the first condition. In an experimental trial day, subjects were asked to take either NAC or PLA one hour before the exercise, and BP and HR were measured after 10 min seated rest in the lab. Subjects were asked to perform RE in the order of LE, SCP, LC, SR, SSP, and LPD with 3 sets of 10 reps at 80% 1RM, with 2 minutes rest between sets and exercises. Due to Valsalva maneuver increasing RPP (Farinatti et al., 2011), inhalation during eccentric action and exhalation during concentric action were used to minimize Valsalva maneuver.

4.2.6 Statistical analysis

The Shapiro–Wilk test was used to verify the data normality, and the Levene test was used to verify the homogeneity of variance. A one-way repeated measure ANOVA was applied to compare the difference on post-exercise RPP, SBP, and HR in 1RM, NAC and PLA, as well as post-exercise RPP for each exercise in 1RM. A two-way repeated-measure ANOVA was applied to compare the difference between rest RPP and post-exercise RPP in NAC and PLA,

and the difference on post-exercise RPP, SBP, and HR for each exercise in 1RM, NAC and PLA. A three-way repeated measure ANOVA was applied to compare the difference of RPP in set, exercise and treatments. A paired t test was applied to compare the RPP_{change} (the percentage change of RPP between post-exercise and rest) between PLA and NAC. Tukey HSD Post Hoc test was performed when necessary. Statistical significance was set at the $P < 0.05$ level. The data were analyzed by using JMP$^{@}$ pro 15 (SAS Institute Inc., Cary, NC, USA). All results were means ± SD.

4.3 Results

There was no significant different between post-exercise RPP in NAC and PLA, and no significant treatment and time effects on post-exercise RPP. However, post-exercise RPPs (NAC: 14.29 ± 2.87 mm Hg · beats · min^{-1}; PLA: 15.39 ± 2.34 mm Hg · beats · min^{-1}) were significantly greater than rest RPPs (NAC: 10.07 ± 2.04 mm Hg · beats · min^{-1}; PLA: 9.46 ± 1.51 mm Hg · beats · min^{-1}) in both treatments (NAC: $P < 0.0005$; PLA: $P < 0.0001$). There was no significant difference on RPP_{change} between PLA (65.02%) and NAC (44.63%) (Figure 4.1).

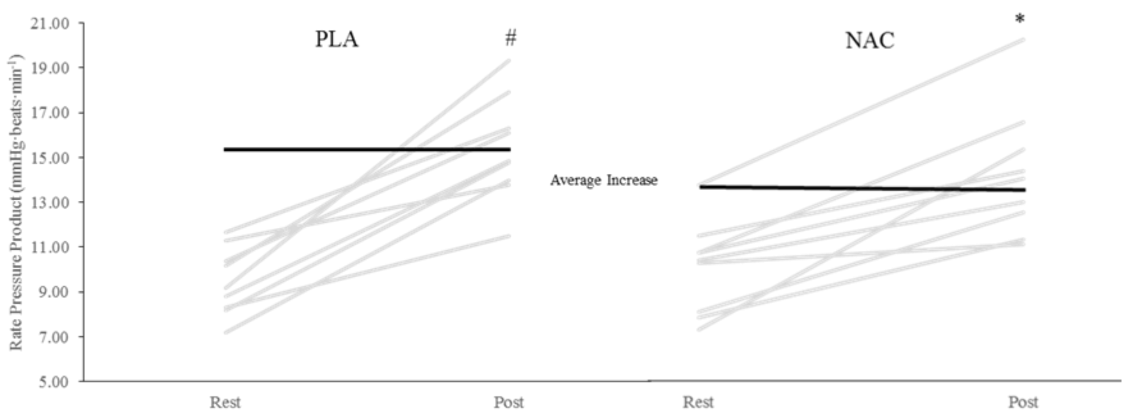

Figure 4.1. Rest and post-exercise RPPs, percentage change of RPP for NAC and PLA (# PLA, $P < 0.0001$; * NAC, $P < 0.0005$).

There were significant differences on post-exercise RPP between 1RM (9.89 ± 1.63 mm Hg · beats · min^{-1}), NAC (13.79 ± 2.76 mm Hg · beats · min^{-1}) and PLA (14.05 ± 2.34 mm Hg · beats · min^{-1}) ($P < 0.0001$), and no significant difference on rest RPP ($P = 0.57$). Post Hoc Tukey test showed post-exercise RPP of 1RM was significant lesser than that of PLA and NAC ($P < 0.0001$), no significant difference between NAC and PLA (Figure 4.2).

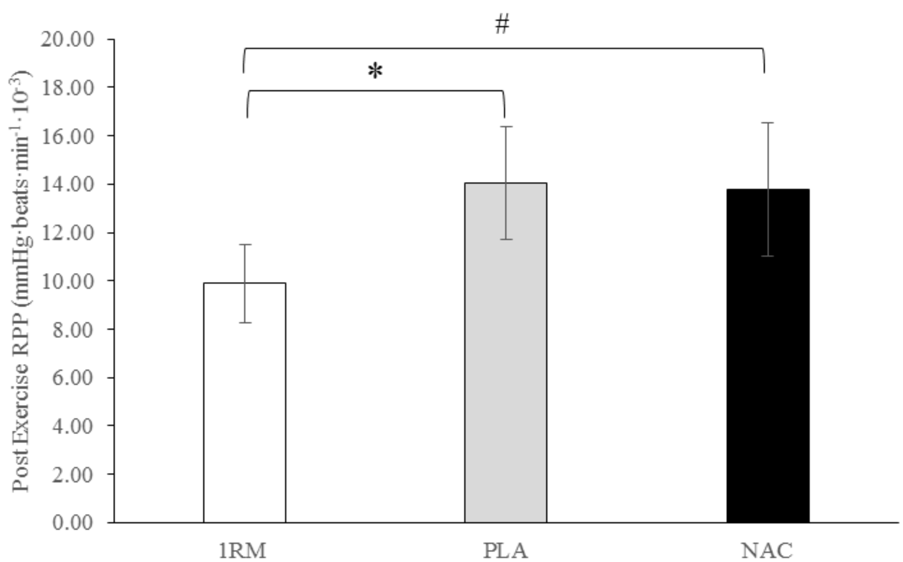

Figure 4.2. Post-exercise RPP of 1RM, PLA and NAC (# 1RM < PLA, * 1RM < NAC, P < 0.0001).

There was no significant difference in post-exercise SBP between 1RM, NAC and PLA ($P < 0.07$). However, post-exercise HR between 1RM, NAC and PLA was significant difference ($P < 0.0001$). Post Hoc Tukey test showed post-exercise HR of NAC (109.02 ± 18.88 beats· min-1), PLA (108.00 ± 16.07 beats· min-1) were significantly greater than that of 1RM test (77.89 ± 7.87 beats· min-1) ($P < 0.0001$). There was no significant difference between NAC and PLA post-exercise HR ($P = 0.91$) (Figure 4.3).

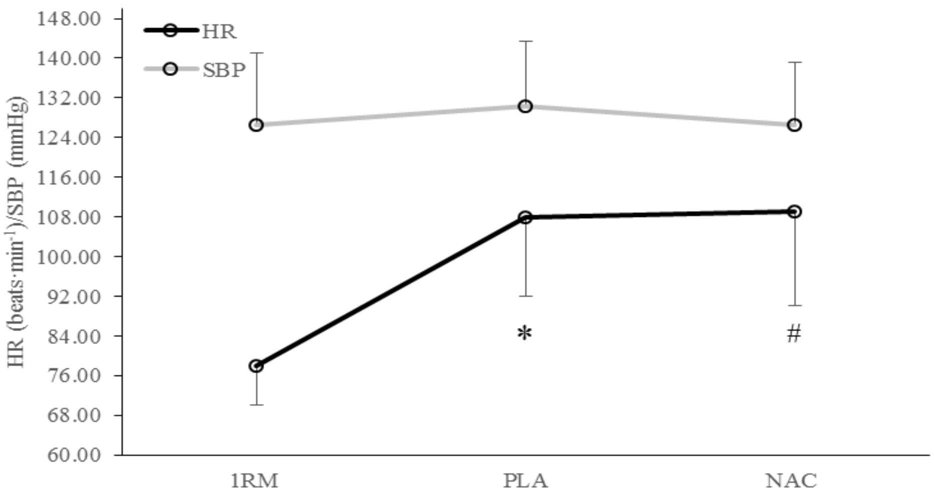

Figure 4.3. Post-exercise HR and SBP of 1RM, PLA and NAC (* 1RM < PLA, # 1RM < NAC, P < 0.0001).

For each exercise, post-exercise RPP demonstrated the same results: PLA and NAC were significantly greater than that of 1RM, with no significant difference between PLA and NAC (Figure 4.4).

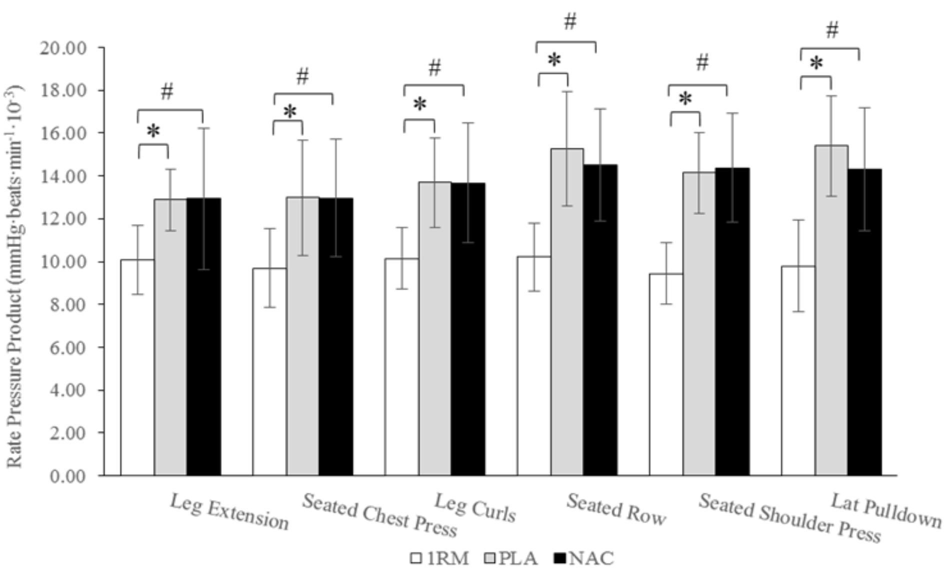

Figure 4. 4. Post-exercise RPPs of 1RM, PLA and NAC for each exercise (# 1RM < NAC, * 1RM < PLA, P < 0.05).

Post-exercise SBP was not significant difference between 1RM, PLA and NAC in almost all exercises, except PLA was greater than 1RM in leg extension exercise (P < 0.05) (Figure 4.5).

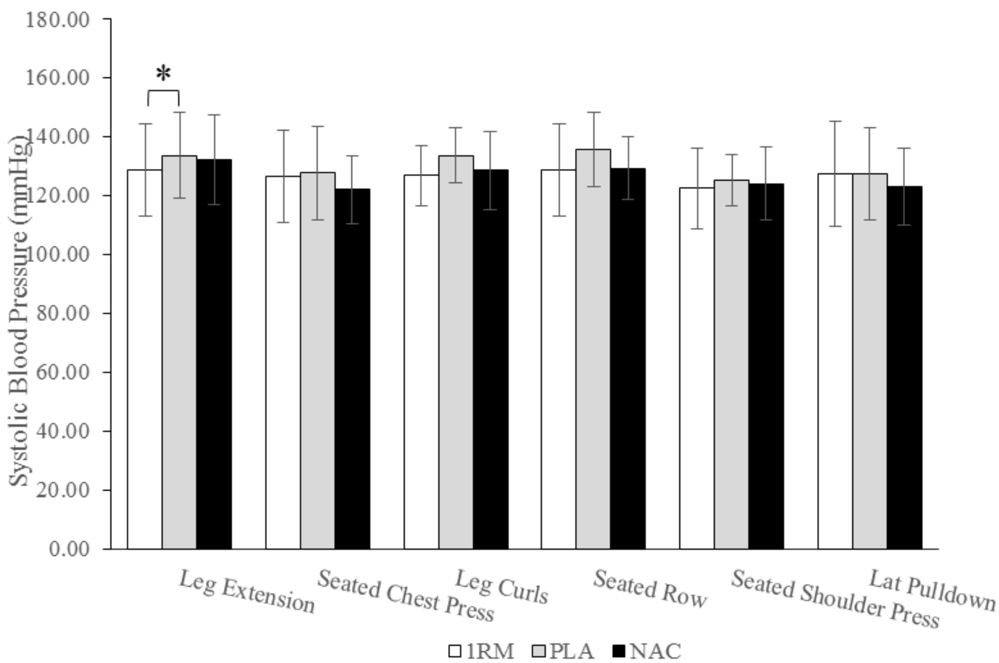

Figure 4.5 Post-exercise SBP of 1RM, PLA and NAC for each exercise (* 1RM < PLA, P < 0.05).

For each exercise, post-exercise HR demonstrated the same results as post-exercise RPP: PLA and NAC were significantly greater than that of 1RM, and there was no significant difference between PLA and NAC (P < 0.05) (Figure 4.6).

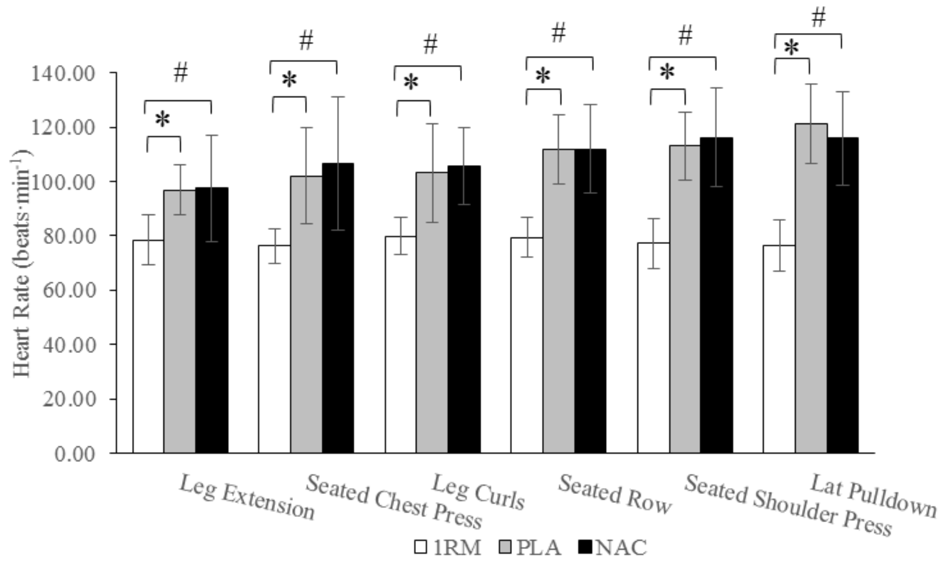

Figure 4.6. Post-exercise HR of 1RM, PLA and NAC for each exercise (# 1RM < NAC, * 1RM < PLA, P < 0.05).

There was no significant difference between post-exercise RPP of 1RM for each exercise (P=0.92) (Figure 4.7).

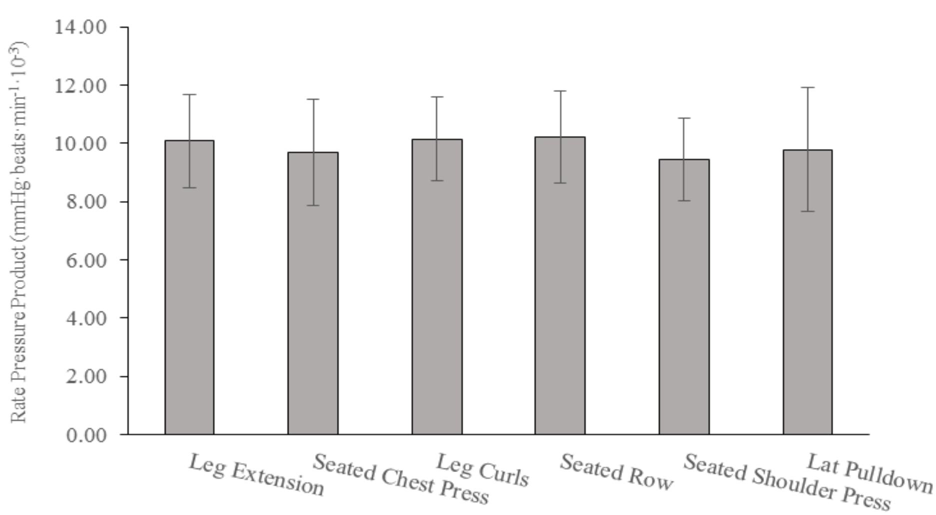

Figure 4.7. Post-exercise RPP of 1RM for each exercise.

There was no significant difference between set RPPs of each exercise for PLA and NAC. However, the RPPs of set 1, set 2, and set 3 were significant greater than that of rest RPP both in PLA and NAC (P < 0.05), there was no significant difference on RPPs between sets both in PLA and NAC (Figure 4.8).

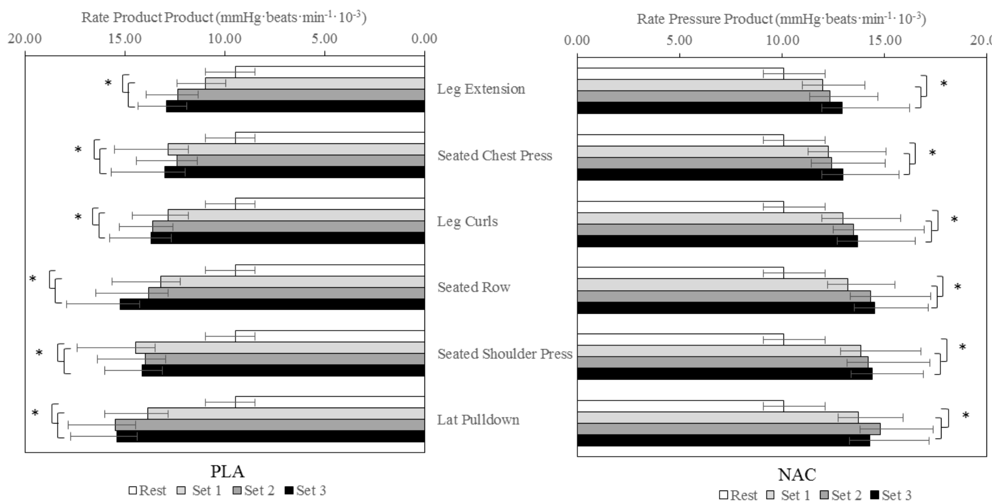

Figure 4. 8. Set RPPs for different exercises in both PLA and NAC groups (* Rest < Set 1, Set 2, and Set 3, P < 0.05).

4.4 Discussion

The main findings of this study were that NAC intake did not significantly decrease post-exercise RPP of regular RE as compared to PLA, both NAC and PLA treatments significantly increased post-exercise RPP over rest RPP. Interestingly, post-exercise RPP for NAC and PLA were significant greater than that of 1RM test, and it was mainly due to increased HR, but not SBP. Furthermore, for each exercise, post-exercise RPP had the same outcomes: it was significantly greater than that of 1RM test both for NAC and PLA, and the effect was due to increase of HR but not SBP. In 1RM test, post-exercise RPP of each exercise was not significantly different. Finally, for each exercise, there was no significant difference of set RPP

between NAC and PLA, but RPPs of set 1, set 2 and set 3 were significantly greater than rest RPP for both treatments.

The main goal of this study was to examine NAC treatment on reducing the stressor effect of regular conventional RE on the heart. However, NAC treatment demonstrated the same effect as PLA, inducing a greater post-exercise RPP as compared to rest RPP, with the similar results evident for every single RE. However, RPP_{change} of NAC (44.63%) was less than that of PLA (65.02%), which indicated post-exercise RPP of NAC was less than that of PLA, although not significantly different. Nieminen et al. (Nieminen et al., 2008) reported $RPP_{recovery}$, calculated as peak RPP minus post-exercise RPP, is a promising candidate for a prognostic marker, with the greater the drop in RPP meaning a lower risk of death. Thus, post-exercise RPP plays an important role in measuring heart stress. However, studies referring $RPP_{recovery}$ to be a prognostic marker measured the post-exercise SBP and HR at different times: 4 min post exercise (Nieminen et al., 2008), 2 and 5 min post exercise (Kiviniemi et al., 2019). Moreover, these indexes measured at 5 min post exercise were more predictive than those measured at 2 min (Kiviniemi et al., 2019). While in the current study, the indexes were measured within 30 seconds after exercise, this may underestimate NAC effect. However, since the rest times for RE are normally from 2 to 3 min, having a 5 min measurement would not mimic this study's desired standard RE program. Thus, in order to find a significant effect of NAC on post-exercise RPP, measuring SBP and HR at 5 min post each exercise or completion of the whole exercise bout may provide more reliable information. Human studies investigated NAC treatment on RE have shown to delay fatigue during knee-extension exercise (Koechlin et al., 2004), and repetitive submaximal handgrip exercise (Matuszczak et al., 2005), but the current study was the first study to investigate NAC treatment on stress effect of RE on the heart. The inconsistency could be

ascribed to the way the drug was administrated. First, in a study by Andrews et al. (Andrews et al., 2001), NAC was infused in coronary at 48 mg · min^{-1} for 10 min to an intra-arterial concentration of 2 mol/L. On the other hand, in the current study, 1800 mg NAC was orally administrated. Thus, the intra-arterial concentration of NAC may not have reached the level of 2 mol/L. The other reason could be due to the dosage, even though the daily dosage was 1800 mg in the current study was similar as previous studies (Koechlin et al., 2004; Matuszczak et al., 2005), the drug was administrated for 4 and 3 days respectively in previous studies, instead one day in the current study. Taken altogether, in order to draw a consistent conclusion, a dosage of NAC reaching the intra-arterial concentration of 2 mol/L, or 1800 mg/day for at least 3 days may be needed.

In the current study, a post-exercise RPP being significantly greater than rest RPP in NAC and PLA treatments, was in agreement with previous studies (da Silva et al., 2007; Iglesias-Soler et al., 2015; Maior et al., 2014c). However, the previous results were based on the studies conducted on non-regularly performed RE, and the current study was the first to examine an acute effect of regular conventional RE on RPP. Scholars tried to use RPP as a prognostic factor to predict heart events. The threshold for silent ischemic events could be as low as 10 to 14 mm Hg ·beats · min^{-1} in patients with hypertension (Uen et al., 2003). However, many other studies supported a greater RPP value. The cutoff for the highest sensitivity specificity for prognostic significance of myocardial infarction can be 21. 70 mm Hg · beats · min^{-1} (Villella et al., 1999), an average of 23. 2 mm Hg · beats · min^{-1} can trigger angina pain (Robinson, 1967). Moreover, a peak RPP less than 36 mm Hg · beat · min^{-1} is considered safe in clinical situations or cardiac rehabilitation programs (Jenny et al., 2008), and it can be range from 25 to 40 mm Hg · beat · min^{-1} for healthy individuals (Fletcher et al., 2001). In the current study, the post-

exercise RPP for NAC and PLA were 13.79 ± 2.76 mm Hg · beats · min^{-1} and 14.05 ± 2.34 mm Hg · beats · min^{-1} respectively. Therefore, a conventional regular RE exerts a low stress pressor on the heart and is thus safe to healthy population.

Post-exercise RPPs of NAC and PLA were significantly greater than that of 1RM test, similar results were evident in every single exercise as well. The 1RM test is determined by raising the maximal weight possible in a single maximum effort and complete movement, aims to stimulate the maximum strength by the practitioner (Horvat et al., 2003). This will exert a great stress effect on the heart, maximal blood pressure was reported to exceed 480/350 mm Hg for seated double-leg press to failure exercise at 1RM (MacDougall et al., 1985). It is reasonable to speculate that 1RM resistance exercise test may induce a great heart stress effect, namely a greater RPP. However, in the current study, post-exercise RPP of 1RM (9.89 ± 1.63 mm Hg · beats · min^{-1}) was significantly less than that of both NAC (13.79 ± 2.76 mm Hg · beats · min^{-1}) and PLA (14.05 ± 2.34 mm Hg · beats · min^{-1}), which was contrary to previously speculated that 1RM would lead to a greater increase of RPP. In the current study, regular RE was 3 sets of 10 repetitions at 80% 1RM and rest for 2 min between set and exercises. While during the 1RM test, total exercise sets were 3-5 sets, repetitions were 1, 3 to 8 at 50%, 80% and 100% 1RM, the rest time between sets and exercises was 1 minute and 5 minutes respectively. The RPP response during RE is directly related to intensity of effort, the number of repetitions and sets, the rest interval, and time of muscle recruitment (de Salles et al., 2010). To this point, 1RM test may exert a less tress effect on the heart as compared to regular RE. However, in the current study, statement should be cautious about 1RM test is safer than that of regular REs, only if the peak RPP is available.

Most interestingly, SBP and HR played a different role on the greater RPP in NAC and PLA as compared to 1RM test. There was no significant difference on SBP between NAC, PLA and 1RM test, while HR was significantly greater in NAC and PLA than that of 1RM test, and the similar results were evident in every single exercise as well. In the other words, HR played a vital role on RPP during RE. The result was contrary to the previous study that large increase in BP in submaximal resistance exercise as compared to 1RM lift (Lovell et al., 2011). The inconsistency could probably be ascribed to exercise repetitions: only 10 repetitions in the current study compared to 15 repetitions in the previous study. It has been shown that BP and HR responses to resistance training are related to the duration of exercise (Lamotte et al., 2005). Furthermore, when measured between the three treatments for each exercise, SBP was not significantly different. This could be explained by a previous study (Lewis et al., 1985), where that the magnitude of pressor response was directly related to active muscle mass in dynamic weight-training exercises. In the current study, the active muscle mass involved in each exercise was similar which resulted in no change in SBP between treatments. However, since the mechanisms responsible for the post-exercise BP response are unclear (Lovell et al., 2011), many studies are needed in the future. On the other hand, HR was significantly greater in NAC and PLA than that in 1RM test, which was in agreement with previous studies (DeVan et al., 2005; Iglesias-Soler et al., 2015; Lovell et al., 2011; O'Connor et al., 1993), this was contrary to the previous statement that SBP may contribute more than HR to the increase in RPP during RE (Graves & Franklin, 2001). The increase HR can be ascribed to the reduction of oxygen supply to active muscles in high-intensity RE causing accumulation of local metabolites, stimulation of chemoreceptors and increased HR and cardiac contractility (Moreira et al., 2017), the increases in HR, myocardial contractility, and sympathetic activity act to augment MVO_2 (Berne, 1964).

Moreover, other studies indicated that increase in HR mainly mediated the augmentation of cardiac output for severe exercise (Franklin et al., 1959), the tachycardia of exercise accounts for approximately one-third of the increment in coronary flow during severe aerobic exercise (Vatner et al., 1972). Therefore, HR reduction is indeed critical to reduce exercise-induced ischemia by increasing subendocardial myocardial blood flows and diastolic perfusion time (Guth et al., 1987), and by decreasing MVO_2 (Colin et al., 2003). Taken altogether, a given increase in the RPP might have different implications depending on whether that increase was due to a rise in HR, or a rise in SBP (Goldstein & Epstein, 1973). Thus, the observation of HR or BP alone does not guarantee client safety, and RPP should be used for evaluation and prescription of exercise (Simonson & Wyatt, 2003). Additionally, since the importance of reduction HR during RE, nutraceuticals claiming to reduce HR should be examined with RE in the future studies.

RPP response to RE is related to recruited muscle mass, lower limbs induce a higher RPP value (Maior et al., 2014a), this because the muscle mass recruited in the exercise blocks the circulation partially and consequently rise in the vascular resistance, leads to increase in BP (MacDougall et al., 1985). In the current study, however, the RPP for each exercise in 1RM test was not significant difference, though upper and lower limb exercises were performed separately. Thus, involved muscle mass could not be the only one factor affected RPP in the current study, more studies are needed in the future. Moreover, studies have found a cumulative effect of exercise set on RPP response (Gotshall et al., 2001; Maior et al., 2014a), but in the current study, no significant difference was found as well, all exercise set RPPs were significant greater than rest RPP. However, debates are emerging to these previous statements. Gotshall et al. (Gotshall et al., 2001) drew the conclusion on the speculation that the increased BP with each

successive set. Maior et al. (Maior et al., 2014a) used different intensity for each set as of 25%, 50%, and 75% 1RM individually, thus, exercise intensity played an obvious effect on the accumulative effect. Thus it is hard to make solid statement to support the accumulative effect of RE on RPP.

Some limitations existed in the current study. First, only 9 subjects finished the study which was less than the expected 13 participants. However, the Cohen effect size was 0.71, thus, it was enough to get the predicted result. Second, SBP and HR were measured within 1 min post exercise, a 5 min post-excise measurement may find out a positive effect. A conventional RE program is time consuming, however, it involves 3-4 sets of 8 to 15 reps for 6-8 exercises, resting for 2-3 min between sets. Thus, a financial aid project to ensure a group of committed subjects would be helpful. Third, the BP was measured indirectly by an auscultatory method, and it could be 29.0 mm Hg less than that measured by catheter (Rasmussen et al., 1985). While direct intra-arterial BP determinations can fully characterize the BP response to RE, there is significant risk associated with this invasive technique such as pain, arterial spasm, blood clots, bleeding, and vasovagal syncope (Gotshall et al., 2001). However, using the auscultation method is possible to identify the relative cardiac overload caused by different exercises. The advantages include accessibility, cost, and non-invasiveness (Maior et al., 2014a). Moreover, the two methods have a very high degree of correlation (coefficient of correlation = 0.95 for SBP) (Holland & Humerfelt, 1964). Therefore, the auscultatory measurement could be considered an appropriate method because a high correlation to direct measurement and many advantages over direct measurement. Lastly, only young and healthy subjects were recruited in the study, patients with chronic diseases such as heart diseases, and diabetes may be sensitive to NAC. Therefore, study may be needed to investigate on this group of population.

In summary, orally intake N-acetylcysteine does not have a significant acute effect on reduction of post-exercise RPP in a regular conventional RE. The important finding is HR plays a vital role in increasing heart stress during RE, HR reduction is critical to reduce exercise-induced heart events. 1RM test induces a less increase of RPP as compared to regular RE, it may be safer than regular conventional RE. However, both 1RM test and regular conventional RE produce a lower RPP values less than that may trigger a heart event, thus, they are safe to most population. RE does not have a cumulative set RPP effect and muscle mass involvement effect for RPP is not evident. For the sake of participants' safe, these findings may help exercise scientists put more attention on monitoring HR instead of SBP, though RE is safe to most population.

CHAPTER 5. CONCLUSION

The purpose of this dissertation was to investigate the acute effect of different types of RE on heart metabolism, and to examine the effect of conventional RE on heart metabolism in combination with nutraceuticals, through measuring RPP. Three studies were conducted to investigate the stress effect of single-set and multiple-set RE, single bout RE and conventional RE on the heart, and the changing stress effect of these REs on heart when combing with nutraceuticals. The first study (Chapter 2) was to examine the effect of volume-matched single-set and multiple-set leg press exercise on myocardial energy expenditure. It was found that post-exercise RPP, RPP_{diff}, RPP_{perc}, and HR_{perc} for single-set were significantly greater than that of multiple-set RE, when performing 4 sets of 10 repetitions or 40 repetitions of leg press exercise at 150% body weight. This result showed single-set RE exerts a greater stress on the heart, and it is suggested that the single-set and multiple-set RE can prescribe to different populations with varied training goals.

The second study (Chapter 3) was designed to investigate Muscle Sentry®, a supplement, its claimed effect on improving work performance and cardiovascular efficiency. No treatment effect was found on either total work performed or estimated MVO_2 between treatments, when subjects performed 3 sets to failure chest and leg pressure exercises at 8 RM. These results showed Muscle Sentry® intake 40 min prior to doing RE had no effect upon either total lift numbers or estimated MVO_2, and suggests that, in some instances, the benefits of Muscle Sentry® are less than those claimed by the manufacturer.

The third study (Chapter 4) was designed to investigate the acute effect of NAC on cardiovascular responses to regular RE, and effect of conventional RE on the heart metabolism.

Compared to previous studies, this study recruited 6 conventional REs, which are commonly performed in regular exercise program, with 3 sets of 10 repetitions at 80% 1RM, with 2 min rest between sets and exercises. There was no significant treatment effect on RPPs. Post-exercise RPP of conventional RE was significant greater than of 1RM test. Instead of SBP, post-exercise HR of conventional RE significantly increased among treatments and 1RM test. These results suggest NAC does not have an acute effect on reduction of post-exercise RPP in a conventional RE training program. Additionally, HR, not SBP, plays a vital role in increasing heart stress during conventional RE. Moreover, a 1RM test is safer for a healthy population as compared to conventional RE.

In summary, the potential risk of RE posed on the heart of an increasing heart workload, may place susceptible individuals in danger. In this dissertation, RE does increase post-exercise RPP, but this rise falls within the safe range. Therefore, conventional RE can be safe for most of the population, especially healthy individuals. Moreover, HR, not SBP, plays a vital role in increasing RPP, and it should be monitored during the RE. The nutraceuticals examined in the dissertation did not show benefits on the heart stress. More studies are needed in the future to investigate whether any nutraceuticals claiming to reduce HR actually have an influence upon the heart's metabolic load.

APPENDIX A. STUDY PROTOCOL

Title: Acute Effect of Conventional Resistance Exercise in Conjunction with N-Acetylcysteine on Rate Pressure Product

Experimental Overview

The experiment is a randomized crossover design, in which all subjects will be treated with either placebo (Psyllium fiber: PLA) or supplement (N-acetylcysteine: NAC) when performing a conventional RE program. The conventional RE program includes leg press (LP), seated chest press (SC), leg curl (LC), seated row (SR), seated shoulder press (SP), and lat pull-down (LPD). All exercises will consist of 3 sets of 10 reps at 80% 1RM, with 2 minutes rest between sets. Subjects will come to lab for a total 5 times: 1) a strength fitness trial, 2) a familiarization trial, 3) a 1RM test trial, and 4) &5) treatment trials. Each session will be conducted on the same time of the day for each subject, and the interval between sessions will be at least 48 hours for trials 1-3 and one week for trials 4 & 5. In the experimental trials, subjects will be given either the placebo or the supplement 1 hour before the resistance exercises. Once arriving in the lab, each subject will rest by sitting quietly for 10 minutes, SBP and HR measured on left arm by the same research personnel using an automated device. Then, they will start to perform six conventional REs. The SBP and HR testing will be repeated right after the last rep of each exercise.

Participants

Approximately 30 college students (age range = 19-30) enrolled in LSU Kinesiology resistance exercise classes will be recruited to participate in the project. Inclusion criteria: healthy, normotension (<120/80 mm Hg), no nutraceuticals or medication intake for more than

one year, and no supplementations of any kind throughout testing. Exclusion criteria include: pre-hypertension (Between 120/80 mm Hg and 139/89 mm Hg), hypertension (>140/90 mm Hg), cardiovascular disease and/or obesity (BMI >30.0). All potential participants will complete the Physical Activity Readiness Questionnaire (PAR-Q) before inclusion into the study. Only those individuals who answer "no" to all questions will be used as research participants. In addition to be qualified, the participant must be currently engaged in a minimum of 30 minutes of resistance exercise twice a week and be in the good strength fitness category (will be tested by the research personnel).

Testing Procedure

On day one, subject will go through the strength fitness testing. Six exercises will be used in this test: lat pull-down, leg extension, bench press, sit-up, leg curl, and arm curl. The amount of resistance is the product of subject's weight (pounds) × percent of body weight (pounds). Each subject is asked to perform the maximum continuous number of repetitions possible, based on the repetitions performed, the percentile rank of each lift can be obtained. Thus, an overall strength fitness category can be determined by an average percentile score for all six exercises. On day two, the subject will go through all six REs without loading under the direction of the examiner. Day three for 1RM test, subjects will perform a specific warm-up set of 8 repetitions at approximately 50% of the estimated 1RM followed by another set of 3 repetitions at 70% of the estimated 1RM. Subsequent lifts will be single repetitions of progressively heavier weights until failure. Each subject will have a maximum of five 1RM attempts of each exercise with one minute rest between attempts. The testing order will be LP, SC, LC, SR, SP, and LPD. The rest interval between each 1 RM test will be no shorter than 5 minutes. Day 4 and 5 are experimental trials are the same as mentioned above.

Instruments

1) Leg press machine, chest press machine, leg curl machine, seated row machine, shoulder press machine, and lat pull-down machine with the brand name Body Master (Rebirth Fitness, Hauppauge, NY).
2) Omron BP710 for SBP and HR (Omron Healthcare, Inc., Bannockburn, IL)

Strength Fitness Measure Tables

Table 1. Resistance Lifting Table

Lift	Percent of Body Weight	
	Men	Women
Lat Pull-Down	0.70	0.45
Leg Extension	0.65	0.50
Bench Press	0.75	0.45
Sit-Up	0.16	0.10
Leg Curl	0.32	0.25
Arm Curl	0.35	0.18

Table 2. Muscle Strength and Endurance Scoring Table

MEN						
Percentile Rank	Lat Pull-Down	Leg Extension	Bench Press	Sit-Up	Leg Curl	Arm Curl
99	30	25	26	30	24	25
95	25	20	21	26	20	21
90	19	19	19	23	19	19
80	16	15	16	17	15	15
70	13	14	13	14	13	12
60	11	13	11	12	11	10
50	10	12	10	10	10	9
40	9	10	7	8	8	8
30	7	9	5	5	6	7
20	6	7	3	3	4	5
10	4	5	1	2	3	3
5	3	3	0	1	1	2

Table cont'd

Women

Percentile Rank	Lat Pull-Down	Leg Extension	Bench Press	Sit-Up	Leg Curl	Arm Curl
99	30	25	27	32	20	25
95	25	20	21	27	17	21
90	21	18	20	22	12	20
80	16	13	16	14	10	16
70	13	11	13	11	9	14
60	11	10	11	6	7	12
50	10	9	10	5	6	10
40	9	8	5	4	5	8
30	7	7	3	2	4	7
20	6	5	1	1	3	6
10	3	3	0	0	1	3
5	2	1	0	0	0	2

Table cont'd

Table 3. Muscle Strength Category

Average Score	Endurance Classification
≥81	Excellent
61-80	Good
41-60	Average
21-40	Fair
≤20	Poor

APPENDIX B. LSU IRB APPROVAL

ACTION ON PROTOCOL APPROVAL REQUEST

LSU

Institutional Review Board
Dr. Dennis Landin, Chair
130 David Boyd Hall
Baton Rouge, LA 70803
P: 225.578.8692
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lsu.edu/research

TO: Arnold Nelson
Kinesiology

FROM: Dennis Landin
Kinesiology

DATE: December 13, 2019

RE: **IRB#** 4316

TITLE: Acute Effect of Conventional Resistance Exercise in Conjunction with N-Acetylcysteine on Rate Pressure Product

New Protocol/Modification/Continuation: New Protocol

Review type: Full ____ Expedited X **Review date:** 12/11/2019

Risk Factor: Minimal X Uncertain ______ Greater Than Minimal______

Approved X **Disapproved**__________

Approval Date: 12/13/2019 **Approval Expiration Date:** 12/12/2020

Re-review frequency: Annually

Number of subjects approved: 30

LSU Proposal Number (if applicable):

By: Dennis Landin, Chairman DLandin

PRINCIPAL INVESTIGATOR: PLEASE READ THE FOLLOWING –
Continuing approval is CONDITIONAL on:

1. Adherence to the approved protocol, familiarity with, and adherence to the ethical standards of the Belmont Report, and LSU's Assurance of Compliance with DHHS regulations for the protection of human subjects*
2. Prior approval of a change in protocol, including revision of the consent documents or an increase in the number of subjects over that approved.
3. Obtaining renewed approval (or submittal of a termination report), prior to the approval expiration date, upon request by the IRB office (irrespective of when the project actually begins); notification of project termination.
4. Retention of documentation of informed consent and study records for at least 3 years after the study ends.
5. Continuing attention to the physical and psychological well-being and informed consent of the individual participants, including notification of new information that might affect consent.
6. A prompt report to the IRB of any adverse event affecting a participant potentially arising from the study.
7. Notification of the IRB of a serious compliance failure.
8. **SPECIAL NOTE: When emailing more than one recipient, make sure you use bcc.**

**All investigators and support staff have access to copies of the Belmont Report, LSU's Assurance with DHHS, DHHS (45 CFR 46) and FDA regulations governing use of human subjects, and other relevant documents in print in this office or on our World Wide Web site at http://www.lsu.edu/irb*

APPENDIX C. STUDY CONTENT FORM

1. Study Title:

Acute Effect of Conventional Resistance Exercise in Conjunction with N-Acetylcysteine on Rate Pressure Product

2. The purpose of this study is to investigate the impact that resistance exercise with intake of N-acetylcysteine on myocardial oxygen consumption. This study will take place over a period of 6 months, you are expected to come the lab for 5 times and 1 hour for each. The first 3 times include strength fitness testing, familiarization trial and 1RM testing with 6 resistance exercises. The last 2 times are experimental trails, you will take supplements either N-acetylcysteine (3 capsules) or placebo (3 capsules) to perform a resistance exercise training protocol consisted of 6 exercises, during the process, the systolic blood pressure and heart rate will be tested.

3. Risks: Participation in the resistance exercise may result in muscle soreness 24-72 hours after completion of the activities. This muscle soreness can lead to a feeling of mild to moderate pain and discomfort for the 24-72 hours.

4. Benefits: Subject will gain knowledge about testing 1RM and measurement of SBP during exercise.

5. Alternatives (if applicable): There are no alternatives to any part of the study. If you do not want to do any part you will be excluded from the entire study.

6. Investigators: The following investigator is available for questions about this study. Dr. Arnold Nelson, Wk: 578-3114, Hm: 766-4621. Junhai Xu, Cell: (225)288-5382, jxu23@lsu.edu.

7. Performance Site: Room 22 Hatcher Hall of Louisiana State University

8. Numbers of Subjects: 30

9. Inclusion Criteria: College students between the age of 19 and 30, who currently are engaged in a minimum of 30 minutes of resistance exercise twice a week and are in good strength fitness. The individual must be healthy, normotension (<120/80 mm Hg), no nutraceuticals or medication intake for more than one year, and no supplementations of any kind throughout testing. To participate in the study, you must meet the requirements of both the inclusion and exclusion criteria.

10. Exclusion Criteria: Individuals who have pre-hypertension (between 120/80 mm Hg and 139/89 mm Hg), hypertension (>140/90 mm Hg), cardiovascular disease and/or obesity (BMI >30.0). Anyone who answers "yes" to any question on the PAR-Q form. Anyone whose strength fitness is below good.

11. Right to refuse: Subjects may choose not to participate or to withdraw from the study at any time without penalty or loss of any benefit to which they might otherwise be entitled.

12. Privacy: Results of the study may be published, but no names or identifying information will be included in the publication. Subject identity will remain confidential unless disclosure is required by law.

13. Signatures:

The study has been discussed with me and all my questions have been answered. I may direct additional questions regarding study specifics to the investigators. For injury or illness, call your physician, or the Student Health Center if you are an LSU student. If I have questions about subjects' rights or other concerns, I can contact Dennis Landin, Institutional Review Board, (225) 578-8692, irb@lsu.edu, or www.lsu.edu/research. I agree to participate in the study described above and acknowledge the investigator's obligation to provide me with a signed copy of this consent form.

Subject signature: ___________________________________ Date: ________________

The study subject has indicated to me that he/she is unable to read. I certify that I have read this consent form to the subject and explained that by completing the signature line above, the subject has agreed to participate.

Subject signature: ____________________________________ Date: ________________

14. Your information collected as part of the research, even if identifiers are removed, may be used or distributed for future research.

Yes, I give permission____

Signature

No, I do not give permission____

Signature

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VITA

Junhai Xu was born in Wendeng, China. Junhai received his bachelor's degree in Physical Education in June of 1999 from Shandong Sport University. In 2002, Junhai graduated with a master's degree in Physical Education & Sports Coaching from Beijng Sport University, China. Upon graduation, he worked as a lecturer in Central University of Finance & Economics, Beijng, China. In 2010, Junhai received his second master's degree in Fitness and Human Performance from University of Houston Clear-Lake, USA. After moving back to China, Junhai worked as a strength and conditioning coach for several Chinese national youth basketball teams, helped those teams win several Asian Basketball Championships within 4 years. Despite the great success, Junhai decided to continue his education in the area of exercise physiology. In 2015, Junhai was admitted as a PhD student in the School of Kinesiology at Louisiana State University, under the mentorship of Dr. Arnold Nelson. Upon graduation, Junhai will receive the Doctor of Philosophy in Kinesiology from the Graduate School at Louisiana State University, and he will continue to devote his enthusiasm for research and teaching for improving exercise performance and health.