J Musculoskelet Neuronal Interact 2013; 13(1):105-110

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Original Article

Is exercise-induced muscle damage susceptibility body segment dependent? Evidence for whole body susceptibility

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Abstract

Objective: The current study examined serum CK activity following bench press (BP) and leg press (LP) exercise-induced muscle damage to evaluate agreement of subjects classification as either high (HiR) or normal responders (NoR) between upper and lower body muscle groups. **Methods:** Forty-two men performed two resistance exercise bouts (BP and LP) of four sets of maximum repetitions to concentric failure at 10RM, following a random design. **Results:** Fourteen subjects were classified as HiR after the BP and thirteen subjects after LP, while nine subjects were classified as HiR for both exercises. The analysis revealed good agreement (Kappa=0.528, with SE=0.137 and 95% confidence interval: from 0.259 to 0.798). Additionally, we found a significant moderate correlation (r=0.65, p<0.001) between CK peaks obtained following LP and BP. **Conclusion:** Our results suggest that exercise-induced muscle damage susceptibility is a whole body characteristic and is not body segment dependent. Thus, it may be that genetic or systemic mechanisms explain individual variation in muscle damage susceptibility.

Keywords: Muscle Damage, Resistance Exercise, Creatine Kinase, Bench Press, Leg Press

Introduction

It is been demonstrated that resistance exercise causes micro muscle damage with associated changes in levels of serum muscular enzymes[1,2]. The primary muscle enzyme serum activity examined after exercise is creatine kinase (CK). The study of CK in sports medicine results in information regarding the state of muscle, since it has been used as a biomarker of muscle damage. But the blood CK elevation response following exercise is characterized by considerable heterogeneity as prior studies have demonstrated large inter-individual variability[3-5].

To study this variability, numerous studies have proposed the use of cut-off values of serum CK elevation after exercise to identify subjects with an exaggerated magnitude of exercise-induced muscle damage[3-7]. Subjects with an exaggerated magnitude have been classified as high responders (HiR) and the mechanisms of this greater susceptibility to exercise-induced muscle damage are not totally understood. Recent studies have proposed that the CK response could depend on gender[2], age[8], training status[9], muscle fiber composition[10], and genetic characteristics[5].

Saka et al. (2009)[11] compared the magnitude of muscle damage after an isokinetic protocol of maximal eccentric exercise of the elbow flexors (EF) and knee extensors (KE) and found the magnitude of muscle damage was greater for EF than KE. They concluded that this difference could be related to the greater total eccentric work per muscle unit in EF and/or to the mechanical features of each muscle group. Other studies have

The authors have no conflict of interest. No external funding was received to develop this study. Study conducted at the Universidade Iguaçu (UNIG) Campus V.

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Edited by: J. Rittweger
Accepted 13 January 2013

also shown that upper body exercise results in greater levels of serum CK and muscle soreness than lower body exercise[12,13].

Chen (2006)[3] demonstrated that CK elevation classification remains the same across time. In their study, 50 subjects performed 30 eccentric actions at 80% of pre-exercise maximal isometric force, then 24 of the 50 were brought back to the laboratory 1 year after the first session to perform the same exercise bout. They showed that the magnitude of CK response was attenuated, but subjects maintained their 1st session classification. We have not found similar studies using lower body exercise.

Interestingly, to our knowledge, there are no studies that have investigated if the CK response to exercise is body segment dependent. Therefore, a lack of knowledge exists regarding if the CK response of the whole body or of the same individual is different between body segments. We hypothesized that, if CK response to exercise is a whole body characteristic, there would be good agreement between serum CK activity following upper body and lower body exercises. Thus, the aim of this study was to investigate the agreement rate of CK elevation response classification (high responder [HiR] or normal [NoR]) between upper and lower body exercise.

Material and Methods

Subjects

Forty two men, who had not participated in regular exercise training (i.e., resistance, endurance or sports training) in the past year, provided informed consent to participate in this study that was approved by the Institutional Ethics Committee. Subjects indicated that they were not currently using medical drugs, dietary supplements, or anabolic steroids, and were without joint, muscular or cardiovascular disease. More specifically, none had a recent history (within the last 3 years) of muscle or joint injuries, and all subjects were apparently healthy. Subjects were tested in five separate cohorts (5 to 10 subjects at a time) at different times for approximately one year. All subjects claimed to be familiar with the bench press and leg press exercises prior to the experiment. None of the subjects were competitive athletes and most were college or university students (Medicine, Physiotherapy, Pharmacy, Psychology, etc.). Subjects were divided according to a computer generated randomization process to initiate the experimental protocol with bench press (BP; n=21) or leg press (LP; n=21). Comparisons of both initial protocol groups prior to strength testing revealed no significant difference in age, height, or body mass.

Procedures

Prior to the experimental exercise sessions, subjects were tested on two separate days to determine a 10 repetition maximum (i.e. 10 RM) for the bench press or leg press according to previous randomization. To minimize possible errors in the 10 RM assessments, the following strategies were employed: (a) all subjects received standard instructions on exercise technique, (b) exercise technique was monitored and corrected as needed, c) body position was held constant (i.e. hand width during BP and foot position during the LP test); and (d) all subjects received verbal encouragement. All 10 RM assessment procedures were performed according to Kraemer & Fry (1995)[14]. Reliability for BP (ICC=0.8665) and LP (ICC= 0.9814) have previously been shown to be excellent[15].

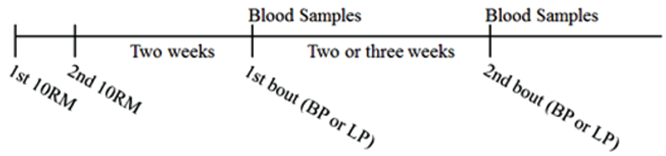

Figure 1. Timeline.

Two weeks following the 10 RM assessments, resistance exercise bouts were performed for each specific group. Two or three weeks later, a similar bout was performed with the exercise changed (i.e., those who performed BP were changed to LP, and *vice versa*) (see timeline showed in Figure 1). All tests were performed in the morning (from 0800 to 1100 h). Subjects were permitted to consume water *ad libitum*, and there were no nutritional recommendations provided after the exercise session.

Exercises were performed for four sets of maximum repetitions to concentric failure with a 10 RM load, with a 2-minute rest interval between sets. The repetition cadence was controlled with a digital sound signal (Beat Test & Training, CEFISE, Nova Odessa, Brazil) that was adjusted so that each repetition was completed in approximately four seconds (2 seconds concentric and 2 seconds eccentric). A researcher observed all exercises performed, and failure was defined as the inability to maintain the cadence or to complete the concentric portion of a lift.

Subjects provided blood samples in a seated position from the antecubital vein into plain evacuated tubes after an 8 h overnight fast prior to each exercise bout, and at 24, 48, and 72 h following exercise. Samples were allowed to clot for 30 min, and then centrifuged at 1600 g for 10 min. The serum was removed, and the serum CK activity was analyzed with an enzymatic method at 37°C (CK-UV NAC-optimized; Biodiagnostica, Pinhais, Brazil) in a Cobas Mira Plus analyzer (Roche, Basel, Switzerland). The CK analyses were made in triplicate and demonstrated high reliability (ICC=0.98).

Statistical Analyses

Following blood analysis, subjects were separated into high responders (HiR) or normal responders (NoR) according to their peak serum CK activity 24 h to 72 h following each bout. Therefore, two peak CK values were obtained, one for the BP bout and another for the LP bout. Specifically, the HiR subjects were classified based on a 90% confidence interval (CI) of peak serum CK activity for each bout (i.e. BP>753.9 U/L; or LP>461.5 U/L).

To evaluate any differences in CK peaks between bouts for each condition (BP-LP or LP-BP) a student t test (Alpha level

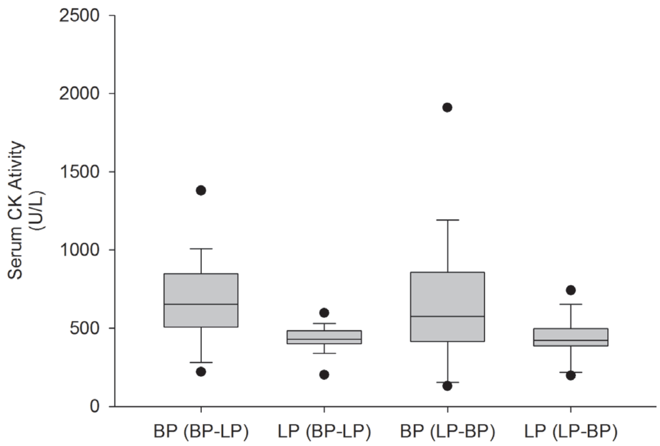

Figure 2. Serum CK peaks by exercise and time (mean±SD). BP1 - peak result after bench press bout, when the bench press was the 1st bout (i.e., BP-LP); BP2 - peak result after bench press bout, when the bench press was the 2nd bout (i.e., LP-BP); LP1 - peak result after leg press bout, when the leg press was the 1st bout (i.e., LP-BP); LP1 - peak result after leg press bout, when the leg press was the 2nd bout (i.e., BP-LP).

	Total	HiR	NoR	P
Age (years)	21.9±4.2	22.2±4.5	21.5±4.4	0.278
Height (cm)	176±6	176±5	176±6	0.291
Weight (kg)	74.4±10.7	74.2±10.1	73.2±10.5	0.286

Table 1. Subject characteristics (mean±SD).

Subject	BP CK peak (U/L)	LP CK peak (U/L)	HiR in both tests
3	584.0	514.0*	
8	438.0	686.0*	
11	779.0*	458.0	
14	1003.0*	494.0*	*
16	1197.0*	502.0*	*
17	930.0*	410.0	
18	788.0*	434.0	
19	870.0*	490.0*	*
20	924.0*	433.9	
21	939.0*	453.0	
23	1330.0*	596.0*	*
25	1419.0*	488.0*	*
28	705.0	523.0*	
29	973.0*	471.0*	*
30	1164.0*	514.0*	*
31	929.0*	510.0*	*
32	1990.0*	748.1*	*
41	534.3	599.0*	

Number of observed agreements was 37 (80.43% of the observations); number of agreements expected by chance: 26.9 (58.51% of the observations).

Table 2. Classification of high responders (HiR) after bench press (BP) and Leg press (LP). * represents HiR classification.

0.05) was performed. The McNemar test was used to compare classifications between BP and LP and the Kappa statistic was performed to determine consistency among classifications. A two-way mixed model analysis of variance (2 groups x 4 times) with repeated measures was used to compare the serum CK peaks between HiR and NoR after each exercise bout (i.e., bench press and leg press separately). Mauchly's test of sphericity was performed with a Greenhouse-Geisser adjustment used when necessary. Multiple comparisons were made with Bonferroni's correction. Additionally, correlations between CK peak following BP and LP bouts were determined by Pearson correlation coefficients.

SPSS-software (version 17.0) was used for all statistical analyses except the Kappa test (used GraphPad Prism v5.00 [GraphPad software, USA]). Results are given as means and standard deviations.

Results

Comparison between groups did not demonstrate any significant differences in age, height or weigtht (Table 1).

First we evaluated any differences in CK peaks between bouts for each condition (BP-LP or LP-BP) to see if there was an influence of the repeated bout effect[16]. There were no significant differences between peaks (p>0.05) (Figure 2).

Subsequently, we separated the high responders (HiR) as classified by peak CK after the BP or LP bout, independent of the order in which they were performed (Table 2). There were 14 HiR after the BP bout (8 being among those who performed the BP in the first bout). There were 13 HiR after the LP bout (8 being among those who performed the LP in the first bout). Additionally we found that 9 subjects were classified as HiR in both situations (5 being among those who performed the BP first). The McNemar test revealed no significant differences between the results (p=1.000), i.e., both tests were statistically satisfactory to classify HiR. The agreement analysis revealed a Kappa=0.528, with SE=0.137 and 95% confidence interval: from 0.259 to 0.798. Thus, the strength of agreement is considered 'good'[17].

Serum CK activity was elevated throughout the 72 h following exercise, with differences expressed in subjects classified as HiR or NoR for both exercises (Figure 3). As expected, serum CK activity demonstrated a significant main effect for group (i.e., HiR vs NoR) ($F_{1,160}$=78.94, p<0.0001 for BP; $F_{1,160}$=34.40, p<0.0001 for LP) and time ($F_{3,160}$=49.79, p<0.0001; $F_{1,160}$=88.47, p<0.0001 for LP) for both exercises. Additionally, a significant group x time ($F_{3,160}$=17.03, p=0.0001 for BP; $F_{3,160}$=9.26, p<0.0001 for LP) interaction was evident for both exercises. Post hoc analysis revealed significant increases in serum CK activity 24 hours after the bout of exercise for both groups and conditions (BP and LP) (p<0.05),

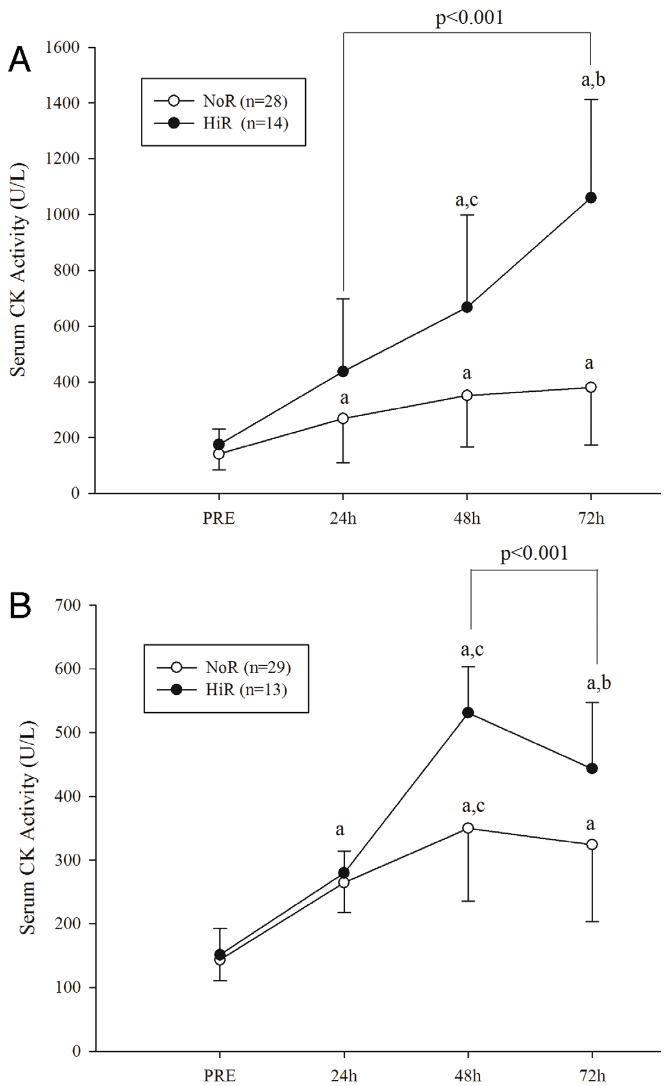

Figure 3. Serum CK activity following bench press (upper) and leg press (lower). (**a**) Denotes differences from PRE (p<0.05); (**b**) denotes differences from PRE (p<0.05); (**c**) denotes differences from 24h.

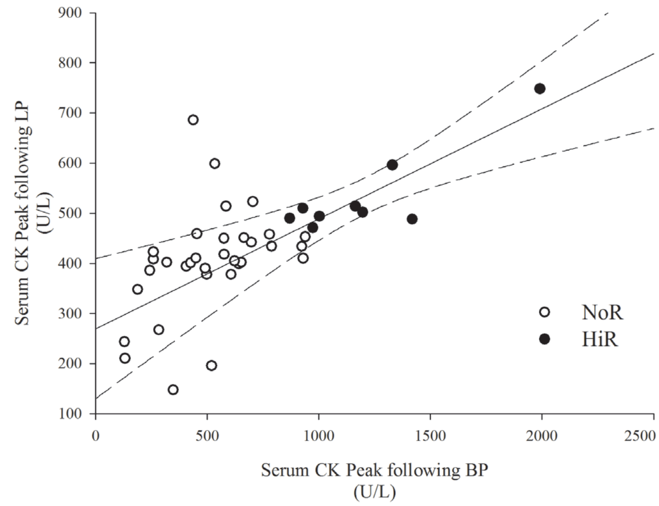

Figure 4. Relationship between serum CK peak following Bench Press (BP) and Leg Press (LP). Pearson correlation coefficient was 0.65 (p<0.001).

except for NoR after LP. There was also a significant difference between groups in CK levels at 24, 48 and 72 h after BP, while after the LP, there were significant differences only at 48 and 72 hours after exercise.

There was a significant moderate correlation ($r=0.650$, $p<0.001$) between the CK peaks obtained after LP and BP (Figure 4).

Discussion

The main finding of this study was an acceptable agreement of the classification of subjects as either HiR or NoR following bench press and leg press fatiguing exercise. This indicates that responder classification is a characteristic of the whole subject, and it does not vary with a change in muscle group or exercise type. This data also sheds light on the inter-individual variability of serum CK activity. These results could support the supposition that genetic or systemic mechanisms are involved in the clearance of CK from the bloodstream, but further studies are necessary to confirm this, since our experimental design was not developed to test this hypothesis.

It has been well documented that an initial bout of exercise confers protection against muscle damage during a subsequent bout performed several weeks later; this is often referred to as the repeated bout effect (RBE)[16]. The present study chose an interval of >14 days between bouts, as previous studies[1,2] showed that markers of muscle damage (muscle soreness, range of motion and CK activity) return to baseline levels within 14 days following resistance exercise. It is important to note that there was no observed RBE in our study, since the serum CK increases were similar for the first and second bouts of each exercise. Additionally, we did not find differences between CK responses when subjects performed BP or LP first; this provides evidence against a crossover effect when one bout of lower body exercise was performed before one bout of upper body exercise (and vice versa). This is a relevant methodological issue because a crossover effect is an unviable method to check if the classification pattern of HiR or NoR can be confirmed for the two exercises types.

Our results corroborate previous studies that demonstrate upper body exercise results in greater peak serum CK activity when compared with lower body exercise[11-13]. Because of the different architecture of arm and leg muscles[18], it is probable that mechanical stress per muscle unit differs between these two muscle groups when performing exercises at the same intensity. This may be one of the reasons for different muscle damage responses. In addition, Jamurtas et al. (2005)[13] proposed that submaximal eccentric actions of lower body muscles, such as downhill walking and descending stairs, are routinely performed during daily activities. It is well documented that, following repeated bouts of eccentric exercise, the muscles adapt to protect against further damage[19] lending support to the proposition of previous investigators[11,13].

We found a good relationship of peak CK between BP and LP exercise (r=0.65, p<0.001). This reinforces our hypothesis that elevation of serum CK activity following exercise is an individual response, in opposition to it being a local response. Despite differences in muscle group characteristics, demonstrated by different CK levels, the individual characteristic of CK elevation was similar across subjects. Serum CK activity is a net result of release by the muscle and clearance by the reticuloendothelial system. This release depends on lymph flow velocity because CK has a molecular weight that does not permit passage directly to the blood. Different velocities for release and clearance could help explain inter-individual CK response variability.

Our results may lead to speculation that determination of CK activity response (i.e., HiR or NoR) following different resistance exercises (i.e., bench press, leg press) may serve to classify subjects for other resistance exercises. As we employed a statistical methodology to classify subjects as HiR or NoR, we do not have a universal cut-off value. This methodological approach allows the classification of HiR following resistance exercises performed with either muscle group, while the classifications based on pre-established cut-off values as used by Clarkson and Ebbeling (1988)[6] serve only for specific muscle groups and actions (i.e., upper body exercise with eccentric muscle actions). Therefore, our methodological approach to identify subjects with greater exercise-induced muscle damage susceptibility (i.e., HiR classification) seems to have greater practical application.

Rhabdomyolysis is a negative event that could be initiated by damaging exercises, such as resistance exercise[18]. It is caused by a variety of mechanisms, ranging from direct muscle injury to genetic and biochemical influences that alter the integrity of muscle cell membranes[21]. Subjects classified as HiR are prone to rhabdomyolysis following resistance exercise[21] and our results reinforce the hypothesis that genetic or systemic mechanisms are involved in the genesis of rhabdomyolysis. Recently, protective strategies have been proposed to avoid excessive risks when HiR subjects perform resistance exercises[21,22].

In conclusion, we found that upper body resistance exercise results in greater peak CK activity than lower body exercise. However, subjects classified as HiR have a greater serum CK activity response independent of the muscle group exercised.

Acknowledgement

The authors would like to thank the volunteers for their participation in this study.

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