Short Recovery Augments Magnitude of Muscle Damage in High Responders

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ABSTRACT

MACHADO, M. and J. M. WILLARDSON. Short Recovery Augments Magnitude of Muscle Damage in High Responders. *Med. Sci. Sports Exerc.*, Vol. 42, No. 7, pp. 1370–1374, 2010. **Purpose**: To examine serum creatine kinase (CK) activity after resistance exercise bouts with different rest intervals between sets and exercises in high responding (HR) and normal responding (NR) subjects. **Methods**: During each resistance exercise bout, three sets with 10-repetition maximum (10RM) loads were completed for the chest press, cable pulldown, biceps curl, triceps extension, leg extension, and prone leg curl. Each bout differed in the length of the rest interval between sets and exercises, specifically either 1 or 3 min. After blood analysis, subjects were separated into NR or HR on the basis of the peak serum CK activity being in the 90th percentile. **Results**: The volume completed (load × sets × repetitions) was significantly greater for the 3-min bout versus the 1-min bout, with no significant differences between the HR and the NR groups. For the NR group, serum CK was significantly elevated from 24 to 72 h after each bout, with no significant differences between bouts. Conversely, for the HR group, the 1-min bout resulted in serum CK activity levels that were approximately 70% greater than the 3-min bout at the 48- and 72-h time points. **Conclusions**: The key finding from the current study was that the HR group experienced significantly greater CK responses when using shorter rest intervals between sets. Conversely, for the NR group, CK responses were not significantly different between bouts. These findings may have implications for resistance exercise prescription in that some individuals might be less tolerant of shorter rest intervals between sets with greater skeletal muscle microtrauma. **Key Words:** REST INTERVAL, EXERCISE VOLUME, SKELETAL MUSCLE MICROTRAUMA, MUSCULAR STRESS, BIOCHEMICAL MARKERS

It is well established that resistance exercise can induce skeletal muscle microtrauma and temporary impairment of muscle function (6,9,13,21). Research on resistance exercise–induced skeletal muscle microtrauma (4,9), sex-specific responses (19), and overtraining syndrome (17,18) has highlighted the importance of recovery periods after high-intensity resistance exercise bouts (3,4,13). In this regard, resistance exercise variables must be carefully prescribed in relation to frequency, volume (i.e., load × sets × repetitions), and the rest interval between sets to reduce the risk of overtraining.

Without periodized prescription of such variables, lifters may exert themselves to such an extent as to induce exertional rhabdomyolysis (ERB), a condition caused by excessive damage to muscle tissue, which promotes delayed-onset muscle soreness, weakness, and increased blood levels of muscle proteins such as creatine kinase (CK), lactate dehydrogenase, and myoglobin (2,12). Although CK and other intramuscular proteins are cleared from the blood by the reticuloendothelial system, myoglobin is cleared by the kidneys. High blood myoglobin levels will first "spill over" into the urine, resulting in myoglobinuria, which may ultimately result in acute renal failure, especially when in environmental conditions of heat stress and dehydration (5,22).

Serum CK response has been studied extensively, and it is considered a qualitative marker for skeletal muscle microtrauma (4–6,13,19). Some individuals tend to exhibit disproportionate increases in serum CK activity after exercise and have been defined as high responders (HR) relative to normal (or low) responders (NR). A clinical or case definition of HR versus NR currently does not exist, and the causation for the disproportionate response in HR is not clearly understood; however, there might be a potential genetic association between HR and serum CK activity (7,20).

Several lines of evidence suggest that the CK-MM-*Nco*I single-nucleotide polymorphism in the 3′-untranslated region might be associated with differential CK-MM activities in myocytes (7). For example, Heled et al. (7) found in

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Submitted for publication October 2009.
Accepted for publication November 2009.

0195-9131/10/4207-1370/0
MEDICINE & SCIENCE IN SPORTS & EXERCISE®

DOI: 10.1249/MSS.0b013e3181ca7e16

88 moderately active subjects a significantly higher percentage of the AA genotype in an HR group versus a significantly higher percentage of the G+ genotype in an NR group (HR vs NR: AA 78% vs 36%, and G+ 22% vs 64%, respectively). Also, 19.4% of the participants with the AA genotype were defined as HR compared with only 3.8% of the participants with G+ genotype.

Heled et al. (7) hypothesized that CK-MM attempts to maintain energy homeostasis by providing a steady supply of creatine phosphate, which is critical for sustaining the function of the ATP–creatine phosphate energy pathway (1,7). A plentiful supply of CP may allow for increased muscle work, but the result might be greater damage to the sarcolemma and, thus, elevated serum CK activity in HR individuals who possess the CK-MM gene. In this regard, the rest interval between resistance exercise sets could be a critical prescriptive variable when considering that approximately 3 min is necessary for complete CP resynthesis between sets of high-intensity resistance exercise (1).

To our knowledge, no studies have been conducted to examine serum CK responses with different rest intervals between sets in those classified as HR or NR. There is a need for research to examine the role of different rest intervals between sets on serum CK activity on the basis of differences in responsiveness. Therefore, the purpose of the current study was to examine serum CK activity after resistance exercises bouts with 1- versus 3-min rest intervals between sets for subjects classified as HR and NR. We hypothesized that serum CK activity would be higher for the 1-min bout in those classified as HR, and there would be no differences in serum CK activity between bouts in those classified as NR.

METHODS

Experimental approach to the problem. Serum CK activity was examined using a randomized within-subjects design during which two resistance exercise bouts that varied only in the length of the rest interval between sets and exercises, specifically 1 or 3 min. Serum CK activity was assessed before each bout and at 24, 48, 72, and 168 h after each bout. Subjects were separated into HR or NR according the peak serum CK activity (CK_{peak}) after each bout, respectively.

Subjects. Thirty-two trained men volunteered to participate in the current study. All subjects were healthy (no muscle, cardiovascular, and joint problems) and were not using ergogenic substances or any other drugs. The purpose and procedures of the experiment were explained, and consent was obtained before the commencement of the experiment. All subjects had been participating in a structured resistance training program for a minimum of 12 months with a mean frequency of three sessions per week, using approximately 30-s to 3-min rest intervals between sets and exercises. All procedures were approved by the local ethics committee. The purpose and procedures were explained to the subjects, and informed consent was obtained according to the Declaration of Helsinki and the norms of the local ethics committee.

Experimental protocol. To control for the repeated bout effect on serum CK activity, two familiarization sessions were conducted in accordance with McHugh (11). During the familiarization sessions, 10-repetition maximum (10RM) loads were assessed for the chest press, cable pulldown, biceps curl, cable triceps extension, leg extension, and prone leg curl (Righetto, Brazil). To increase the reliability of 10RM assessments, the following strategies were used: (a) the 10RM for each exercise was measured on two nonconsecutive days that were separated by 72 h, (b) exercise testing proceeded in the same sequence as listed above, (c) exercise technique was monitored and corrected as needed, and (d) all subjects received verbal encouragement. The highest 10RM load measured during the two familiarization sessions was used during the experiment.

One week after the last familiarization session, subjects performed the first of two resistance exercise bouts (separated by 7 d) with either 1- or 3-min rest intervals between sets and exercises. Warm-up before each bout consisted of pedaling for 10 min on a cycle ergometer and dynamic stretching. During each resistance exercise bout, three sets with 10RM loads were completed for the chest press, cable pulldown, biceps curl, triceps extension, leg extension, and prone leg curl. If subjects were unable to complete 10 repetitions on any given set, the supervising investigator provided minimal assistance so that 10 repetitions were completed on all three sets. The repetition cadence for each exercise was controlled with a digital sound signal (Beat Test & Training; CEFISE, São Paulo, Brazil) that was adjusted so that each repetition was completed in 3 s (1-s concentric and 2-s eccentric).

Blood collection and analysis. Subjects provided blood samples in a seated position from the antecubital vein into plain evacuated tubes after 8 h of overnight fast before each bout and at 24, 48, 72, and 168 h after each bout. Immediately after collection, blood samples were centrifuged at 1600*g* for 20 min. The serum was removed, and 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). CK assessments demonstrated high reliability (intraclass $r = 0.87$). CK analyses were made in triplicate and demonstrated high reliability (intraclass $r = 0.99$).

Statistical analysis. After blood analysis, subjects were separated into HR or NR according to the CK_{peak} elicited 24 to 72 h after each bout. Therefore, two peak CK

TABLE 1. Anthropometric data and $CK_{peak}1$ and $CK_{peak}3$ (mean ± SD).

Characteristics	HR (*n* = 7)	NR (*n* = 25)	*P*
Age (yr)	26.4 ± 3.2	23.8 ± 4.2	0.13
Height (cm)	173.0 ± 7.8	176.9 ± 7.2	0.62
Body mass (kg)	72.9 ± 6.0	74.6 ± 8.4	0.23
$CK_{peak}1$	961.7 ± 250.7	320.6 ± 147.1	0.01*
$CK_{peak}3$	698.0 ± 172.2	297.9 ± 140.4	0.01*

* Significant difference between HR and NR ($P < 0.05$).

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TABLE 2. ICC and CV 10RM tests.

Exercise	ICC	CV
Chest press	0.7941	15.9
Cable pulldown	0.6428	10.8
Biceps curl	0.8209	22.8
Triceps extension	0.8196	22.8
Leg extension	0.8168	21.2
Prone leg curl	0.8935	15.8

values were obtained, one for the 1-min ($CK_{peak}1$) bout and another for the 3-min ($CK_{peak}3$) bout. The difference between baseline serum CK activity and the peak serum CK activity from 24 to 72 h was used to classify HR versus NR individuals. Specifically, the HR subjects were classified on the basis of serum CK activity in the 90th percentile for each bout (i.e., $CK_{peak}1 \geq 556.2$ $U \cdot L^{-1}$ or $CK_{peak}3 \geq 442.3$ $U \cdot L^{-1}$). Only subjects who met the inclusion criteria for both bouts (i.e., 1 and 3 min) were classified as HR (7). On the basis of this criterion, 7 (i.e., ~22%) of the 32 subjects were classified as HR.

The reliability of the 10RM loads for each exercise and CK assessments was assessed with the intraclass correlation (ICC) and the coefficient of variation (CV). The volumes completed (load × sets × repetitions) for each exercise were compared between the HR and NR groups using paired *t*-tests. To compare serum CK activity, a 2 (groups) × 2 (rest interval) × 5 (CK assessments) repeated-measures ANOVA was used. The α level was set at less than 0.05 for a difference to be considered significant. Significant main effects were further analyzed using pairwise comparisons with Tukey *post hoc* tests. Statistical analysis was completed using SPSS 15.0 for Windows (LEAD Technologies, Haddonfield, NJ).

RESULTS

Anthropometric data and CK_{peak} values are shown in Table 1. Significantly greater CK_{peak} values were demonstrated by the HR group versus the NR group for both rest conditions. There was little variability in demographical characteristics and a high reliability for the 10RM loads assessed for each exercise (Table 2).

Significantly greater volume (load × sets × repetitions) was completed for all exercises during the 3-min bout versus the 1-min bout. However, volume was not significantly different between the HR and NR groups, irrespective of the rest interval condition (Table 3).

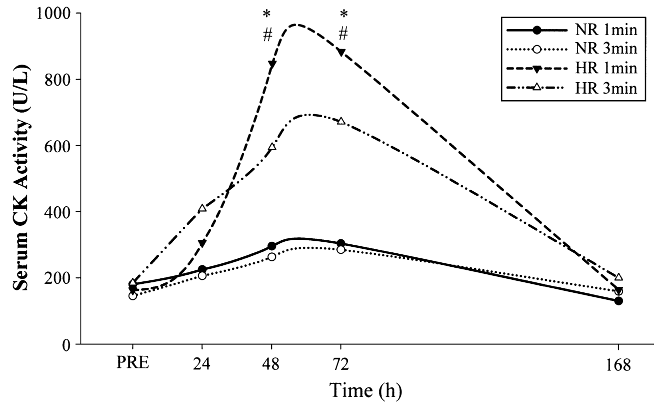

FIGURE 1—Serum CK activity before (PRE) and at 24, 48, 72, and 168 h after the 1- and 3-min bouts in HR (*n* = 7) versus NR (*n* = 25) groups. *HR group had significantly greater CK activity at the 1- versus 3-min bout (*P* < 0.05). #HR group had significantly greater CK activity versus the NR group at the 1- and 3-min bouts (*P* < 0.05).

The HR group exhibited significantly greater serum CK activity versus the NR group at the 48-h (1 min, $P = 0.01$; 3 min, $P = 0.01$) and the 72-h time points (1 min, $P = 0.01$; 3 min, $P = 0.01$). Furthermore, the HR group exhibited serum CK activity levels that were approximately 70% greater after the 1-min bout versus the 3-min bout at the 48-h ($P = 0.03$) and the 72-h ($P = 0.03$) time points (Fig. 1).

DISCUSSION

No clinical or physiological criteria have been established to define the serum CK activity at which an individual would be considered an HR. The magnitude of serum CK response may depend on age, gender, muscle mass involvement, genetics, and intensity of the exercise bout (2,5–7,20,27). Serum CK activity in apparently healthy subjects might be correlated with physical training status and the ability to sustain high levels of muscle tension that results in sarcomeric damage (6,20). In the current study, the exaggerated response in the HR group may have been due to the differences in genetic factors, muscle fiber type, an underlying myopathy, or musculoskeletal fitness level (22).

In the current study, 7 of 32 subjects were classified as HR. Because no consensual clinical criteria exist, for the purpose of this study, HR subjects were classified on the basis of serum CK activity in the 90th percentile ($CK_{peak}1 \geq 556.2$ $U \cdot L^{-1}$; or $CK_{peak}3 \geq 442.3$ $U \cdot L^{-1}$). Only subjects

TABLE 3. Total volume per exercise (kg ± SD).

	NR (*n* = 25)			HR (*n* = 7)		
Exercise	1 min	3 min	*P*	1 min	3 min	*P*
CP	1059.2 ± 260.9	1299.0 ± 267.0	0.01*	1150.0 ± 256.6	1431.4 ± 313.7	0.01*
CPD	940.0 ± 156.5	1108.7 ± 194.2	0.01*	764.3 ± 132.7	929.3 ± 149.5	0.01*
BC	561.3 ± 143.3	710.7 ± 191.2	0.01*	477.4.3 ± 113.3	631.7 ± 133.3	0.01*
TE	677.4 ± 215.2	877.6 ± 245.4	0.01*	524.6 ± 167.2	684.1 ± 167.2	0.01*
LE	1264.5 ± 362.0	1426.4 ± 406.9	0.01*	1088.3 ± 239.7	1289.4 ± 234.9	0.01*
PLC	927.7 ± 225.0	1176.1 ± 275.7	0.01*	970.4 ± 221.3	1161.6 ± 221.3	0.01*
Total	5405.8 ± 824.9	6567.5 ± 886.8	0.01*	4975.0 ± 595.9	6127.6 ± 504.0	0.01*

* Significant difference between 1- and 3-min bouts (*P* < 0.05).
BC, biceps curl; CP, chest press; CPD, cable pulldown; LE, leg extension; PLC, prone leg curl; TE, triceps extension.

who met or exceeded the criteria for both bouts (i.e., 1 and 3 min) were classified as HR (7). Despite clear differences in serum CK responses, the HR and NR groups did not differ in the volume (load × sets × repetitions) completed, which is known to be associated with musculoskeletal fitness level (8,26).

These results imply that musculoskeletal fitness level was not a confounder of our experiment, although musculoskeletal fitness level could be associated with different degrees of skeletal muscle microtrauma after resistance exercise. In agreement with this perspective, Skenderi et al. (16) found that serum CK activity after a 246-km run was not correlated with the time for completion of the race, suggesting that musculoskeletal fitness level was not associated with the serum CK response.

The key finding from the current study was that the HR group demonstrated significantly greater serum CK activity after the 1-min bout versus the 3-min bout, whereas the NR individuals did not respond differently between rest conditions. Consistent with our findings for the HR group, Mayhew et al. (10) found that 1-min rest intervals elicited significantly greater serum CK activity. Two bouts of the leg press exercise were performed for 10 sets of 10 repetitions at 65% 1RM with either 1- or 3-min rest intervals between sets. Significant elevations in serum CK activity were demonstrated at 24 h after both rest conditions, with significantly greater elevations for the 1-min bout.

In the current study, the volume (load × sets × repetitions) completed was significantly greater for the 3-min bout. This finding corroborates several previous studies (23–25). Nevertheless, there were no significant differences between the HR and NR groups in the volume completed, despite differing serum CK responses. The NR group demonstrated similar elevations in serum CK independent of the rest condition, a finding that corroborates previous findings of Ribeiro et al. (14) and Rodrigues et al. (15). Conversely, the HR group demonstrated significantly greater elevations in serum CK for the 1-min rest condition. Because the HR and NR groups did not differ in the volume (load × sets × repetitions) completed for each rest condition, other mechanisms were responsible for the exaggerated response in the HR group.

Currently, there is no established connection between an exaggerated CK response and ERB; however, the possibility should not be overlooked. Rhabdomyolysis 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. ERB occurs in response to strenuous physical exertion (e.g., eccentric exercise) that may impose excessive mechanical and metabolic stress on muscle fibers. Serum CK activity is a common marker used to assess the status of muscle fiber membranes, and some individuals (i.e., HR) may exhibit an exaggerated response (2,6,7,20).

The key finding from the current study was that some individuals with greater exercise-induced serum CK activity may have their condition worsened by shorter rest intervals between sets and exercises. Future research should seek to establish a possible connection between an exaggerated serum CK response and ERB. The data from the current study may assist practitioners in prescribing the appropriate rest interval during resistance exercise bouts. Prescribing the appropriate rest interval should be based on training history and the objective of the training program. If an individual does not have a history of consistent training with shorter rest intervals between sets and exercises, then the exercise prescription should evolve slowly to reduce skeletal muscle microtrauma and the potential risk of developing ERB.

No external funding was received to develop this study. This study was conducted at the Universidade Iguaçu Campus V.

The authors thank the subjects who made this study possible and who endured the inconvenience of this investigation. The authors also thank Priscilla Clarkson and Stephanie M. Cole for their helpful comments on the manuscript; Edalmo França, Jr., and Pierre A. Silva for their help in data collection; and Rafael Pereira, Felipe Sampaio-Jorge, and Paulo Azevedo for discussion during data analysis and preparation of the manuscript.

The results of the present study do not constitute endorsement by the American College of Sports Medicine.

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