SHORT INTERVALS BETWEEN SETS AND INDIVIDUALITY OF MUSCLE DAMAGE RESPONSE

MARCO MACHADO,1,2 RAFAEL PEREIRA,3 AND JEFFREY M. WILLARDSON4

1Laboratory of Human Movements Studies, University Foundation of Itaperuna (FUNITA), Itaperuna, Brazil; 2Laboratory of Physiology and Biokinetics, Faculty of Biological Sciences and Health, Brazil; 3Department of Biological Sciences, State University of Southwest Bahia (UESB), Jequié, Bahia, Brazil; and 4Kinesiology and Sports Studies Department, Eastern Illinois University, Charleston, Illinois

ABSTRACT

Machado, M, Pereira, R, and Willardson, JM. Short intervals between sets and individuality of muscle damage response. J Strength Cond Res 26(11): 2946–2952, 2012—This study examined creatine kinase (CK) activity after resistance exercise sessions in subjects classified as high (HiR), medium (MeR), or low responders (LoR). Two resistance exercise sessions were performed that each involved 4 sets of the biceps curl at 85% of a 1 repetition maximum (1RM) and either 1- or 3-minute rest intervals between sets. High responders and MeR demonstrated significantly greater CK activity after the 1-minute session vs. the 3-minute session. Therefore, the HiR and MeR subjects exhibited less tolerance to resting 1 minute between sets, whereas the CK activity was not significantly different between rest intervals for the LoR subjects. The application of these findings indicates the need to vary the length of the rest interval between sets with the understanding that individuals exhibit varying recuperative abilities and some might be less tolerant of shorter rest intervals between sets.

KEY WORDS rest interval, exercise volume, skeletal muscle microtrauma, muscular stress, biochemical markers

INTRODUCTION

Increased activities of muscle-specific enzymes such as serum creatine kinase (CK) have been widely used as indirect indicators of the extent of skeletal muscle microtrauma (1,7,9,19,20,25). After high-intensity resistance exercise, localized microtrauma of the sarcolemma results in leakage of CK into the interstitial fluid, then CK is taken up by the lymphatic system and shuttled into the circulation; blood levels of CK may remain elevated for 2–6 days (1,7,19). This condition, referred to as exercise-induced hyperCKemia, is characterized by considerable heterogeneity because prior studies have demonstrated large interindividual variability in blood CK elevations after exercise (3,9,11,15).

Certain individuals tend to exhibit disproportionate elevations in serum CK activity after exercise and have been defined as high responders (HiR). A clinical or case definition of an HiR does not currently exist and the causation for the disproportionate serum CK activity in HiR is not clearly understood; however, a potential genetic predisposition might be a contributing factor (11,12). Chen (3) demonstrated that certain individuals continued to exhibit disproportionately elevated CK responses for 1 year after their first session of eccentric exercise despite the existence of the “repeated bout effect” (18).

It is well established that resistance exercise can induce skeletal muscle microtrauma and acute impairment of muscle function (7,16,20,24). Research on skeletal muscle microtrauma (4,16) has highlighted the importance of recovery periods of several hours after high-intensity resistance exercise sessions (2,4,20). In this regard, resistance exercise variables must be carefully prescribed in relation to the load, frequency, volume (i.e., load × sets × repetitions), and the rest interval between sets for continued adaptational responses as expressed through gains in strength and hypertrophy.

The rest interval between sets is a key variable that has been the focus of prior research on resistance exercise-induced skeletal muscle microtrauma. Several previous studies have demonstrated insignificant differences in hyperCKemia after resistance exercise sessions that involved 1- or 3-minute rest intervals between sets (14,21,22). However, a recent study (15) demonstrated significantly greater CK activity when resting 1 vs. 3 minutes between sets for subjects classified as HiR, based on the extent of the postexercise CK activity. This study indicated that certain individuals do express greater sensitivity to shorter rest intervals between sets, but further research is necessary to examine CK responses in a larger sample of untrained individuals.

Furthermore, in a population of untrained individuals, it is not currently known whether programming different rest
intervals between sets during a resistance exercise session that involves relatively low muscle mass and low volume (e.g., multiple sets of the biceps curl exercise) would be sufficiently stressful to classify sensitivity to muscle damage as indicated by the individuality of serum CK activity. Such information would be important for coaches to appreciate the importance of progression in programming the length of the rest interval between sets, especially for athletes that might potentially express greater sensitivity to exercise-induced muscle damage. Thus, the research question: Does multiple sets of the biceps curl exercise with different rest intervals between sets represent a sufficiently stressful stimulus to determine sensitivity to muscle damage in untrained individuals?

To answer this question, serum CK activity was compared after biceps curl exercise sessions conducted with either 1- or 3-minute rest intervals between sets, with the intent to classify subjects as being high (HiR), medium (MeR), or low (LoR) in sensitivity. We hypothesized that a relatively low muscle mass and low volume session would induce sufficient sarcolemmal disruption to classify subjects into HiR, MeR, and LoR groups; furthermore, there would be significantly greater CK activity when resting 1 minute between sets for the HiR group.

**METHODS**

**Experimental Approach to the Problem**

Serum CK activity was examined using a randomized within-subjects design during which 2-elbow flexion (biceps curl) sessions were performed that varied only in the length of the rest interval between sets, specifically: 1 or 3 minutes. Serum CK activity was assessed before each session and at 24, 48, 72, and 96 hours after each session. The subjects were classified as low (LoR; <500 IU·L⁻¹), medium (MeR; 500 to <2,000 IU·L⁻¹), or high (HiR; ≥2,000 to 10,000 IU·L⁻¹) responders according to the peak serum CK activity (CKpeak) after both sessions, respectively.

**Subjects**

Fifty men, between 18 and 35 years of age, volunteered to participate in this study. The subjects indicated that they were competitive athletes, and most were university students. The purpose and procedures were explained to the subjects, and informed consent was obtained according to the Declaration of Helsinki after approval from the local Ethics Committee.

**Experimental Protocol**

Two initial familiarization sessions were conducted to establish a reliable 1RM for a machine biceps curl (Righetto, São Paulo, Brazil); these initial sessions were separated by 72 hours. One week after the last 1RM session, the subjects performed the first of 2 resistance exercise sessions (separated by 7 days) with either 1- or 3-minute rest intervals between sets. The rest interval during each session was applied by random assignment for each subject. Warm-up before each session consisted of dynamic stretching and then 2 sets of 15 repetitions with 40% of the 1RM load. During each biceps curl session, 4 sets were performed for maximal repetitions with 85% of a 1RM load. The cadence for each repetition was controlled with a digital sound signal (Beat Test and Training, CEFISE, Nova Odessa, Brazil) and was completed in approximately 3 seconds (1 second for the concentric phase and 2 seconds for the eccentric phase); if the cadence slowed because of fatigue, the subjects were allowed to continue until reaching voluntary exhaustion.

**Blood Collection and Analysis**

All the tests were performed in the morning (from 8 to 11 AM). During the testing sessions, the subjects were allowed to drink ad libitum; throughout the duration of the experiment, the subjects were encouraged to maintain their typical nutritional intake. Blood samples were collected with the subjects in a seated position from the antecubital vein into plain evacuated tubes after an 8-hour overnight fast before each session, and at 24, 48, 72, and 96 hours after each session. Immediately after collection, blood samples were centrifuged at 1,600g for 10 minutes. 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 performed in triplicate and demonstrated high reliability (intraclass r = 0.98).

**TABLE 1. Subject characteristics (mean ± SD).**

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (y)</th>
<th>Body mass (kg)</th>
<th>Height (cm)</th>
<th>1RM (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LoR</td>
<td>22.2 ± 3.9</td>
<td>74.3 ± 9.0</td>
<td>178.8 ± 5.7</td>
<td>36.1 ± 3.9</td>
</tr>
<tr>
<td>MeR</td>
<td>22.6 ± 4.8</td>
<td>75.1 ± 11.2</td>
<td>177.5 ± 7.7</td>
<td>36.9 ± 4.8</td>
</tr>
<tr>
<td>HiR</td>
<td>20.8 ± 3.6</td>
<td>77.4 ± 8.6</td>
<td>179.0 ± 3.2</td>
<td>36.2 ± 4.5</td>
</tr>
</tbody>
</table>

*LoR = low responders; MeR = medium responders; HiR = high responders.*
**Rest Interval and CK Activity**

| Table 2. Repetitions and volume (kilograms) comparison (mean ± SD).* |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| **Repetitions** | **First set** | **Second set** | **Third set** | **Fourth set** |
| **Volume (kg)** | **Total** | **Repetitions** | **Volume (kg)** | **Repetitions** |
|                 | 1 min | 3 min | 1 min | 3 min | 1 min | 3 min | 1 min | 3 min |
| **LoR**         | 9.7 ± 1.6 | 9.7 ± 1.6 | 5.2 ± 1.3† | 5.8 ± 0.9† | 297.2 ± 53 | 298.0 ± 59.2 | 159.3 ± 38.7† | 179.5 ± 38.6† |
| **MeR**         | 9.4 ± 1.3 | 9.4 ± 1.6 | 5.0 ± 1.3† | 5.9 ± 1.2†§ | 295.6 ± 55.1 | 295.7 ± 63.4 | 156.1 ± 44.6† | 184.9 ± 40.6† |
| **HiR**         | 9.4 ± 0.5 | 9.4 ± 0.5 | 5.0 ± 1.0† | 5.4 ± 0.9† | 289.2 ± 38.4 | 289.2 ± 38.4 | 152.5 ± 28.1† | 165.4 ± 29.1† |
| **Volume (kg)** |       |       |       |       |       |       | 159.3 ± 38.7† | 179.5 ± 38.6† |
| **LoR**         | 39.5 ± 23 | 39.5 ± 23 | 39.5 ± 23 | 39.5 ± 23 | 136.9 ± 76.7 | 136.9 ± 76.7 | 136.9 ± 76.7 | 136.9 ± 76.7 |
| **MeR**         | 44.6 ± 0.8 | 44.6 ± 0.8 | 44.6 ± 0.8 | 44.6 ± 0.8 | 123.2 ± 72.3 | 123.2 ± 72.3 | 123.2 ± 72.3 | 123.2 ± 72.3 |
| **HiR**         | 38.4 ± 152.5 | 38.4 ± 152.5 | 38.4 ± 152.5 | 38.4 ± 152.5 | 108.6 ± 59.2 | 108.6 ± 59.2 | 108.6 ± 59.2 | 108.6 ± 59.2 |

*LoR = low responders; MeR = medium responders; HiR = high responders.
†Significantly different vs. the first set for the same group (p < 0.05).
‡Significantly different vs. the second set for the same group (p < 0.05).
§Significantly different 1- vs. 3-minute session (p < 0.05).
[Significantly different from the third set for the same group (p < 0.05).]

The muscle soreness data were assessed using a visual analog scale (VAS) that consisted of a 100-mm continuous line representing “not sore at all” (0 mm) to “very, very sore” (100 mm). The subjects were asked to report their soreness level on the line when the investigator extended the elbow and palpated the biceps brachii (3).

**Statistical Analyses**

The subjects were classified as low (LoR: <500 IU·L\(^{-1}\)), medium (MeR: 500 to <2,000 IU·L\(^{-1}\)), or high (HiR: >2,000 to 10,000 IU·L\(^{-1}\)) responders according to the peak serum CK activity (CK\(_{\text{peak}}\)) after both sessions, respectively. This method was adapted and modified based on studies by Clarkson and Ebbeling (5) and Clarkson et al. (9).

The reliability of the 1RM loads for each exercise and CK assessments was assessed with the intraclass correlation (ICC) and the reliability was described as “excellent” for ICC values in the range of 0.8–1.0 and “good” for 0.6–0.8, whereas values <0.6 were “poor” (23). Dependent variables were assessed with a 2-way mixed model analysis of variance (3 groups × 2 rest interval conditions) with repeated measures over time points and group as between-subject factors to compare the serum CK response, number of repetitions, volume completed per set and per session and muscle soreness for the groups (LoR, MeR, and HiR) after exercise bouts conducted with different rest intervals between sets. The serum CK response to exercise was our main dependent variable, but the number of repetitions and volume completed was included to evaluate differences between groups in exercise performance, whereas muscle soreness was included to give a clinical perception about the exercise-induced muscle damage from groups and bouts. Multiple comparisons were made according to Bonferroni’s method with a significance level of p < 0.05. Statistical analysis was completed using SPSS® 17.0 for Windows (LEAD Technologies, Charlotte, NC, USA).

**Results**

At baseline, there were no differences in the age, body mass, height, or biceps curl 1RM among groups (Table 1). The number of repetitions per set, the volume completed per set, and the total repetitions and volume completed per session are shown in Table 2. The number of repetitions and...
volume completed per set demonstrated a significant main effect for rest interval length ($F_{1,376} = 27.19, p < 0.001$ for the number of repetitions; $F_{1,376} = 20.47, p < 0.001$ for volume completed) and for sets ($F_{3,376} = 325.41, p < 0.001$ for the number of repetitions; $F_{1,376} = 235.31, p < 0.001$ for volume completed). Additionally, the number of repetitions and volume completed per set demonstrated a significant main effect for rest interval length ($F_{1,376} = 27.19, p < 0.001$ to number of repetitions; $F_{1,376} = 20.47, p < 0.001$ to volume completed).

We also found a significant rest interval length $\times$ set interaction ($F_{3,376} = 4.06, p = 0.007$ for the number of repetitions; $F_{3,376} = 2.98, p = 0.031$ for volume completed) for the number of repetitions and volume completed per set. For all the groups (i.e., LoR, MeR, and HiR), the number of repetitions and volume decreased similarly for all 3 groups as indicated by the nonsignificant main effect for group ($F_{2,376} = 1.58, p = 0.208$ for repetitions; $F_{2,376} = 2.31, p = 0.101$ for volume completed), the nonsignificant interaction for group $\times$ rest interval length ($F_{3,376} = 0.542, p = 0.582$ for repetitions; $F_{3,376} = 0.376, p = 0.687$ for volume completed), and the nonsignificant interaction for group $\times$ set ($F_{6,376} = 1.06, p = 0.385$ for repetitions; $F_{6,376} = 0.537, p = 0.780$ for volume completed).
Rest Interval and CK Activity

For all the groups (i.e., LoR, MeR, and HiR), the performance, expressed as the number of repetitions and volume completed per set, decreased over 4 sets and the differences between rest intervals lengths were evident at the second set only for the MeR group, and at third and fourth sets for all the groups. Additionally, the total repetitions and total volume completed per session (sum of repetitions or volume completed over 4 sets) demonstrated a significant main effect for rest interval length ($F_{1,94} = 13.49, p < 0.0001$ for repetitions; $F_{1,94} = 8.28, p = 0.005$ for volume completed). All the groups demonstrated the greatest total repetitions, and total volume completed per session when resting 3 minutes between sets.

As expected, serum CK activity was elevated throughout the 96 hours after exercise, with differences expressed in subjects classified as LoR, MeR, and HiR (Figure 1). Serum CK activity demonstrated a significant main effect for group ($F_{3,470} = 504.30, p < 0.0001$), rest interval length ($F_{1,470} = 19.50, p < 0.0001$), and time point ($F_{2,470} = 248.45, p < 0.0001$). Additionally, significant group × rest interval length ($F_{3,470} = 4.75, p = 0.009$), group × time point ($F_{3,470} = 51.57, p < 0.0001$) and rest interval length × time point ($F_{3,470} = 2.80, p = 0.026$) interactions were evident.

All the subjects maintained their classification (i.e., LoR, MeR, or HiR) irrespective of the length of the rest interval. Furthermore, the MeR and HiR groups, but not LoR group, exhibited significantly higher exercise-induced serum CK activity when the exercise protocol was conducted with 1- vs. 3-minute rest intervals between sets.

The muscle soreness, assessed with a VAS, demonstrated a significant main effect for group ($F_{3,470} = 3.23, p = 0.041$) and time point ($F_{2,470} = 218.77, p < 0.0001$). An increase in muscle soreness was observed at the 96-hour point for all the groups ($p < 0.05$) (Figure 2). Additionally, the muscle soreness was significantly greater for HiR group (both the 1- and 3-minute rest interval sessions) vs. the MeR group, at the 48-hour time point ($p < 0.05$). When the HiR group was compared with the LoR group, a significant difference was observed at the 48-hour time point for the 3-minute rest interval condition ($p < 0.05$).

**Discussion**

The key finding from this study was the significantly greater hyperCKemia induced by a biceps curl session that involved relatively low muscle mass and low volume in untrained individuals. Furthermore, the HiR and MeR groups exhibited significantly greater serum CK activity after the session that involved 1- vs. 3-minute rest intervals between sets. Exercise-induced hyperCKemia has been well described, and the magnitude of the CK response may depend on age, gender, the amount of muscle mass stimulated during exercise, genetics, and the intensity of the loads used during the exercise session (1,6,7,11,24). The level of serum CK activity exhibited after resistance exercise in apparently healthy subjects might be related to physical training status and the ability to sustain high levels of muscle tension that contributes to widespread muscle tissue disruption (7,24).

In this study, 5 out of 50 subjects were classified into the HiR group based on the CK_peak that exceeded previously established criteria (>2,000–10,000 IU/L) after both sessions (i.e., 1 and 3 minutes) (15). Despite clear differences in serum CK responses, the HiR, MeR, and LoR groups did not differ in the volume (load × sets × repetitions) completed, which is known to be associated with musculoskeletal fitness level (13,27). These findings were consistent with those of Evangelista et al. (10) who demonstrated no correlation between the total volume completed and CK_peak after a biceps curl session.

The design used by Evangelista et al. (10) involved similar muscle actions as the current study (i.e., concentric and eccentric), but the intensity was lower (40% the subject’s maximal voluntary isometric contraction strength), and subjects were not classified based on their CK_peak. Therefore, this study adds greater understanding to the existing body of knowledge regarding the individuality of the CK response after resistance exercise because our data indicate that the volume completed was not the key modulator of exercise-induced hyperCKemia.

The results of this study indicate that when HiR and MeR subjects executed the biceps curl session with 1-minute rest intervals between sets, the magnitude of hyperCKemia was significantly greater vs. when 3-minute rest intervals were used between sets, whereas the LoR subjects did not respond differently between rest conditions. Consistent with our findings for the HiR group, Mayhew et al. (17) reported that 1-minute rest intervals between sets elicited significantly greater serum CK activity vs. 3-minute rest intervals between sets after a leg press session that involved 10 sets of 10 repetitions at 65% 1RM.

In this study, the volume (load × sets × repetitions) completed was significantly greater for the 3-minute session for all groups. This finding was consistent with those of several previous studies (10,26–28); nevertheless, there were no significant differences among the HiR, LoR, and MeR groups in the volume completed for each rest condition, despite the significantly different serum CK responses. The LoR group demonstrated similar elevations in serum CK independent of the rest condition, a finding that corroborates previous findings of Ribeiro et al. (21), Rodrigues et al. (22), Machado et al. (14), and Evangelista et al. (10). Conversely, the HiR and MeR groups demonstrated significantly greater elevations in serum CK for the 1-minute rest condition. Because the groups did not differ in the volume (load × sets × repetitions) completed for each rest condition, other mechanisms were responsible for the accentuated responses in the MeR and HiR groups. These other mechanisms may include speed of lowering dumbbell (3); genetic differences between subjects (11,12); differences on reticuloendothelial capacity of CK clearance (5).
With regard to the subjective ratings of muscle soreness, differences were observed between HiR and LoR-MeR groups at 48 hours after exercise. Myofibrillar microtrauma and the associated inflammation are the most likely peripheral mechanisms initiating muscle soreness. It is possible that if muscle inflammation does occur, chemical mediators upstream of prostaglandin synthesis, such as cytokines, would be released into the muscle, contributing to the hyperalgesia. At the present time, no studies have compared interindividual CK activity with physiological markers of inflammation (prostaglandin and cytokines), which could be the focus of future studies. We can only speculate that the significantly greater muscle soreness and serum CK activity after resistance exercise in the HiR group was indicative of greater muscle damage and inflammatory mediators, despite the similar volume completed vs. the MeR and LoR groups for each rest condition.

**Practical Applications**

The key finding from this study was that a biceps curl session that involved relatively low muscle mass and low volume was sufficiently stressful to induce significantly greater serum CK activity in MeR and HiR groups when resting 1 vs. 3 minutes between sets. The application of these findings might indicate the need to vary the length of the rest interval between sets with the understanding that individuals exhibit varying recuperative abilities. Some individuals might be less tolerant of shorter rest intervals as indicated by greater subjective ratings of muscle soreness during the 48 hours after a resistance exercise session. 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 from longer rest intervals (e.g., 3 minutes) to shorter rest intervals (e.g., 1 minute) between sets to allow for gradual adaptation in creating greater resilience to skeletal muscle microtrauma.

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**References**


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