

Greater eccentric exercise-induced muscle damage by large versus small range of motion with the same end-point

AUTHORS: Fochi AG¹, Damas F², Berton R³, Alvarez I¹, Miquelini M¹, Salvini TF⁴, Libardi CA¹

¹ Laboratory of Neuromuscular Adaptations to Resistance Training, Department of Physical Education, Federal University of São Carlos, São Carlos, Brazil

² School of Physical Education and Sport, University of São Paulo, São Paulo, Brazil

³ School of Physical Education, State University of Campinas, Campinas, São Paulo, Brazil;

⁴ Department of Physical Therapy, Federal University of São Carlos, São Carlos, Brazil.

ABSTRACT: Several factors can affect the magnitude of eccentric exercise (ECC)-induced muscle damage, but little is known regarding the effect of the range of motion (ROM) in ECC-induced muscle damage. The purpose of this study was to investigate whether elbow flexor ECC with 120° of ROM (from 60° of elbow flexion until elbow full extension – 180° [120ROM]) induces a greater magnitude of muscle damage compared with a protocol with 60° of ROM (120-180° of elbow flexion [60ROM]). Twelve healthy young men (age: 22 ± 3.1 years; height: 1.75 ± 0.05 m; body mass: 75.6 ± 13.6 kg) performed the ECC with 120ROM and 60ROM using different arms in a random order separated by 2 weeks and were tested before and 24, 48, 72 and 96 h after ECC for maximal voluntary isometric contraction torque (MVC-ISO), ROM and muscle soreness. The 120ROM protocol showed greater changes and effect sizes (ES) for MVC-ISO (-35%, ES: 1.97), ROM (-11.5°, ES: 1.27) and muscle soreness (19 mm, ES: 1.18) compared with the 60ROM protocol (-23%, ES: 0.93; -12%, ES: 0.56; 17°, ES: 0.63; 8 mm, ES: 1.07, respectively). In conclusion, ECC of the elbow flexors with 120° of ROM promotes a greater magnitude of muscle damage compared with a protocol with 60° of ROM, even when both protocols are performed at long muscle lengths.

CITATION: Fochi AG, Damas F, Berton R et al. Greater eccentric exercise-induced muscle damage by large versus small range of motion with the same end-point. *Biol Sport*. 2016;33(3):285–289.

Received: 2016-01-13 ; Reviewed: 2016-02-23; Re-submitted: 2016-02-27; Accepted: 2016-02-27; Published: 2016-07-02.

Corresponding author:

Cleiton Augusto Libardi

Laboratory of Neuromuscular

Adaptations to Resistance

Training / Department of

Physical Education / Federal

University of São Carlos -

UFSCar

Rod. Washington Luiz, km 235

– SP 310, CEP 13565-905,

São Carlos, SP, Brazil

Phone: +55 16 3351-8767

E-mail: c.libardi@ufscar.br

Key words:

Muscle soreness

Lengthening contractions

Resistance exercise

Isokinetic

INTRODUCTION

It is well known that unaccustomed eccentric exercise (ECC) induces muscle damage, which can be indirectly indicated by decreases in strength and range of motion (ROM), and increases in delayed onset muscle soreness [1-3]. The magnitude of muscle damage can be influenced by several factors, such as exercise intensity [4], velocity of movement [5], and muscle exercise [6, 7], among others. However, the influence of some factors that affect the magnitude of muscle damage are not fully understood, such as the influence of total ROM during the ECC (i.e., degree of muscle stretching during ECC).

It has been suggested that the total ROM can affect the magnitude of muscle damage in animals [8, 9]. Brooks et al. [8] showed that passive muscle stretching greater than 50% relative to the muscle fibre size induced larger muscle strength deficits than passive muscle stretching lower than 30%. Additionally, Talbot and Morgan [9] observed a strong correlation between total ROM and muscle damage. Thus, animal studies suggest that the total ROM developed at the ECC may induce a greater degree of muscle injury, which can also be the case for humans.

In humans, Nosaka and Sakamoto [10] compared two protocols for ECC (ROM of 80°), but with different degrees of initial muscle stretching of the elbow flexor muscles (50-130° [small angle condition] vs 100-180° [large angle condition]). The large condition showed a greater decrease in magnitude of muscle damage than the small condition. The same authors also demonstrated with a range of motion of 50° greater magnitude of muscle damage for the large angle condition (100° to 180°) compared to the small angle condition (50° to 130°) [11]. Although muscle damage is greater when ECC begins with elbow flexors more stretched (i.e., large angle, 130-180°), little is known about whether a larger ROM of ECC promotes an even greater magnitude of muscle damage in humans.

To the best of our knowledge, only one study has directly compared the effect of two different total ROMs (20-80° vs. 10-130°) on the magnitude of muscle damage in humans [12]. The results showed greater muscle damage after the ECC with larger compared to small ROM. However, the different velocities [13] and final degree of elongation during ECC [10, 11] per se can affect the magnitude of muscle damage. In addition, only markers of muscle damage (i.e.,

muscle soreness and creatine kinase) with considerable variability between subjects or that may not reflect correctly the magnitude of muscle damage were used [14, 15], which can show even greater variability in inter-subject design.

We propose that comparing different ROMs using a single ECC velocity, the same final degree of elongation (ROM end-point) and also good indirect markers of muscle damage (e.g., maximal voluntary isometric contraction), with a cross-over design (i.e., reducing the inter-subject variability) would increase the precision in measuring the contribution of ROM in muscle damage.

Therefore, the aim of the present study was to investigate the influence of different ROMs on the magnitude of muscle damage when both protocols are matched for velocity of execution and end at the same elbow joint angle. Based on the studies presented above, it is possible to suggest that large ROMs promote greater muscle damage. Thus, our hypothesis is that the larger ROM (120° of total ROM, 60-180°) will promote a greater magnitude of muscle damage compared with the smaller one (60° of total ROM, 120-180°).

MATERIALS AND METHODS

Participants. The sample size was estimated from a sample calculation based on data from a study comparing muscle damage induced by ECC at different angles of the elbow flexors [10]. With an alpha level of 0.05, a power (1- β) of 0.80, and a potential 30% difference in maximal voluntary isometric contraction torque (MVC-ISO) between angles of the elbow flexors two days after the protocol, the analysis showed that at least eight participants in total were necessary for this study. Thus, 12 healthy young men (age: 22 ± 3.1 years; height: 1.75 ± 0.05 m; body mass: 75.6 ± 13.6 kg) volunteered to participate in this study and gave written and informed consent before participation. They had not performed resistance training for the upper limbs in the last six months and reported no history of neurological or orthopaedic injuries in the upper limbs. The study was conducted according to the Declaration of Helsinki, and ethical approval was granted by the ethics committee at the local university.

Experimental design

A randomized within-subjects experimental design (i.e., cross-over trial) was used to test the hypotheses. All participants performed unilaterally the two ECC protocols, with different total ROM (120° [120ROM] and 60° [60ROM]). The order of ECC protocol execution and the limb (dominant and non-dominant) used were randomized to minimize possible interference effects in the results. Participants visited the laboratory on 12 occasions separated by 2 weeks. Three days before and immediately before (Pre) ECC, maximal voluntary isometric contraction torque (MVC-ISO) and range of motion (ROM) were measured for the test-retest reliability (between two baseline measurements). These indirect markers of muscle damage and muscle soreness were re-assessed at 24, 48, 72 and 96 h after ECC to assess the magnitude of muscle damage and recovery kinetics.

Eccentric exercise (ECC)

Participants were positioned on the isokinetic dynamometer (Biodex System 3 Pro, Biodex Medical Systems, Inc., Shirley, New York, USA) chair and their chest and waist were immobilized by straps. They placed the upper arm on a padded support that secured the shoulder joint angle at 90° flexion and 0° abduction. The forearm was kept in the supine position holding the lever attachment of the isokinetic dynamometer. The rotation axis of the dynamometer was visually aligned with the elbow joint. Before the ECC a warm-up of two sets of three repetitions (concentric/concentric) at 90°s⁻¹ was performed. To avoid delay in torque, before each eccentric contraction the subjects performed a 1-s isometric contraction at the initial position in each repetition. The ECC consisted of five sets of six maximal voluntary eccentric contractions of the elbow flexors at an angular velocity of 90°s⁻¹ with a 1-min rest between sets. The return was performed passively at 5°s⁻¹ for 60ROM and 10°s⁻¹ for 120ROM (to assure the same rest interval between repetitions). During ECC, the 120ROM protocol performed 120° of full amplitude, starting from 60° of elbow flexion until 180° of elbow flexion (full extension); and the 60ROM protocol performed 60° of full amplitude, starting from 120° of elbow flexion and ending at the same point (i.e., at 180° of elbow flexion). All participants were also verbally encouraged to perform the maximum effort possible in each eccentric contraction. After the completion of each set, the total work (TW) and peak torque were recorded by the dynamometer software.

Maximal voluntary isometric contraction torque (MVC-ISO)

MVC-ISO of the elbow flexors was measured at an elbow joint angle of 90° in the same position on the dynamometer as that used for the ECC. Participants performed three MVC-ISO, holding each contraction for 3 s with a 30-s rest between contractions. The peak torque of each contraction was obtained, and the higher value of the three trials was used as the MVC-ISO value [7]. The coefficient of variation (CV) value for MVC-ISO was 3.2%.

Range of motion (ROM)

ROM was performed using a metal goniometer (Baseline, Aurora, IL, USA) and determined as the difference in maximal voluntary elbow flexion and extension angles. Landmarks used to measure the elbow joint angles were the lateral epicondyle of the humerus, the palpated distal end of the deltoid muscle, the midpoint between the styloid processes of the ulna and radius, and the styloid process of the radius. Measurements were obtained when subjects extended to its maximum the elbow joint and when they flexed the joint most in an attempt to touch the shoulder with the palm. The measurements were performed three times, always in the limb that performed the ECC. The average of three measurements was computed for further analysis [7]. The CV value for ROM was 1.6%.

Muscle soreness

Muscle soreness of the elbow flexors was measured by a visual analogue scale (VAS) that had a 100-mm continuous line with “no

pain at all” on one end (0-mm) and “unbearable pain” on the other end (100-mm). The elbow joint of the participants was passively extended and flexed throughout its maximal possible range of movement. Then, the subjects were asked to rate their perceived soreness rating on the VAS [7]. Muscle soreness was defined as the value measured on the VAS.

Statistical analysis

To compare between 120ROM and 60ROM for the dependent variables (MVC-ISO, ROM and muscle soreness) at baseline, the TW and eccentric peak torque performed in the ECC, unpaired t-tests were used. The effect size value for comparison between protocols at baseline was also calculated. A mixed model analysis with protocol and time set as fixed factors, and participants set as the random factor, was used to compare the effect of 120ROM and 60ROM protocols in the dependent variables [16]. In the case of significant *F*-values a Tukey adjustment was used for multiple comparison purposes. The peak of change of each dependent variable was calculated for each participant considering the greatest change in each dependent variable after the ECC. Peak values were compared using the unpaired t-test. Effect sizes (ES) were calculated using Cohen’s *d* equation [17] $d = M_2 - M_1 / S_{pooled}$ where *M*₁ and *M*₂ are the means of the peak of change protocols and *S*_{pooled} is the pooled standard deviation. The significance level was set at *P* < 0.05. All results are reported as mean ± standard error of the mean (SEM).

RESULTS

Baseline values for the dependent variables are shown in Table 1. No significant difference between protocols in dependent variables was found at baseline (*P* > 0.05). The total work (TW) was greater for 120ROM compared with 60ROM (*P* < 0.05). However, peak torque was similar (*P* > 0.05) between protocols (Table 1).

There was a significant main effect of time and protocol for MVC-ISO, ROM and muscle soreness (Figure 1). MVC-ISO decreased significantly after ECC (Figure 1A) for both protocols (120ROM [Nm]:

TABLE 1. Baseline values of maximal voluntary isometric contractions torque (MVC-ISO), range of motion (ROM), total work (TW) and eccentric peak torque (ECC-PT) developed in the eccentric exercise in the protocol with 120° of ROM (120ROM) and 60° of ROM (60ROM).

| Variables | 120ROM | 60ROM | Effect size |
|--------------|-----------------|----------------|-------------|
| MVC-ISO (Nm) | 54.83 ± 2.06 | 57.16 ± 2.68 | 0.24 |
| ROM (°) | 146.10 ± 1.48 | 145.02 ± 1.47 | 0.17 |
| TW (J) | 576.46 ± 33.20* | 232.12 ± 14.93 | 2.85 |
| ECC-PT (Nm) | 64.85 ± 3.45 | 60.46 ± 3.03 | 0.30 |

Note: Data shown as mean ± SEM. *Indicates significant difference between protocols (*P* < 0.05).

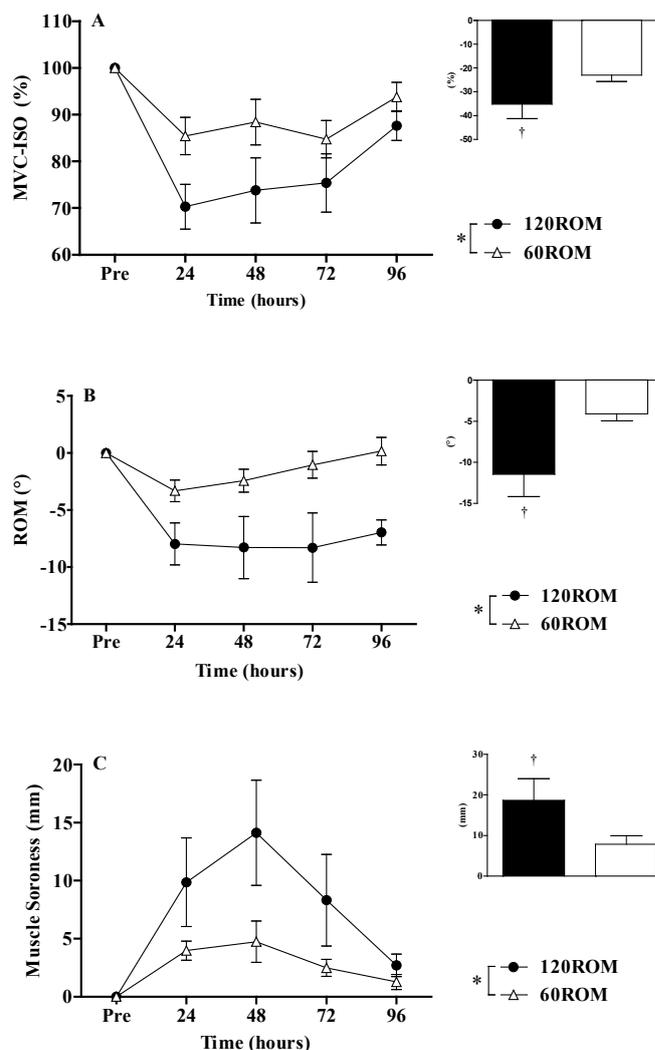


FIG. 1. Normalized changes (mean ± SEM) in maximal voluntary isometric contraction torque (MVC-ISO, pre-exercise = 100%) (A), range of motion (ROM, pre-exercise = 0°) (B) and muscle soreness (pre-exercise = 0 mm) (C) of the elbow flexors before (pre), 24, 48, 72 and 96 h after 120° of ROM (120ROM) and 60° of ROM (60ROM).

Note: Inset: Delta change (pre-to-peak) after 120ROM and 60ROM. *Indicates significant time effect (*P* < 0.05). †Indicates significant difference between protocols (*P* < 0.05).

Pre, 55.00; 24 h, 38.00; 48 h, 39.90; 72 h, 40.81; 96 h, 47.22 vs. 60ROM [Nm]: Pre, 57.10; 24 h, 48.90; 48 h, 49.81; 72 h, 47.70; 96 h, 53.45), and the magnitude of the decrease was significantly greater for 120ROM (-35%; ES: 1.97) compared with 60ROM (-23%; ES: 0.93). As shown in Figure 1B, the ROM decreased significantly after ECC for both groups and the magnitude of decrease was greater for 120ROM (-11.5°; ES: 1.27) compared with 60ROM (-4.1°; ES: 0.63). Muscle soreness increased in both 120ROM and 60ROM (Figure 1C), but the magnitude of increase was significantly greater for 120ROM (19 mm; ES: 1.18) compared with 60ROM (8 mm; ES: 1.07).

DISCUSSION

This was the first study to compare the ECC-induced muscle damage of the elbow flexors in different total ROM protocols, but with the same velocity of movement and ROM end-point (i.e., full elbow extension). The main results confirmed the initial hypothesis that 120° of ROM (120ROM) demonstrated greater magnitude of muscle damage compared with 60° of ROM (60ROM).

Some studies have investigated muscle damage after ECC with different ranges of muscle fibre or whole muscle stretching using animal models. The authors [8, 9] found that the magnitude of stretching can affect the magnitude of muscle damage, as the higher magnitude of stretch promoted greater muscle damage. However, these animal studies should be interpreted carefully, as the sequence of events proposed to lead to muscle damage in an animal model does not necessarily apply to the muscle damage in human muscle after ECC [18]. In humans, only one study has investigated the effect of different total ROMs on the magnitude of muscle damage [12]. Vaczi *et al.* [12] compared two different total ROMs (20-80° vs 10-130°) using 6 sets of 15 knee ECC. However, the protocol that performed greater ROM also performed ECC at greater velocity (120°s⁻¹ for the 120° ROM and 60°s⁻¹ for the 60° ROM) to equalize the total time under tension. Thus, the results showed a greater increase in muscle soreness and CK for the protocol that performed 120° ROM [12]. However, it is known that the velocity of the ECC can affect the magnitude of muscle damage [13, 19]; therefore, both the difference in velocity and the difference in total ROM used in the study [12] could account for their results. In addition, the protocols did not end at the same degree of elongation, which is a major factor that should be accounted for, as the final phase of ROM developed in the ECC is reported to be very important for inducing muscle damage [10]. For instance, it was shown that for the same total ROM (i.e., 80°), the ECC of the elbow flexors performed at a larger angle (100-180° of elbow flexion) promoted greater muscle damage compared with at a smaller angle (50-130° of elbow flexion) [10]. Therefore, for adequately comparing muscle damage after different total ROM eccentric exercises, the experimental design must consider the same exercise velocity and the same ROM end-point. In our study, both protocols performed the ECC with the same extended final elbow joint angle (120-180° of elbow flexion), which is an important factor to consider [10, 11]. By doing that, both conditions (120ROM and 60ROM) had the same stress during maximum elbow extension.

Our results demonstrated no significant difference at baseline for any of the indirect markers of muscle damage between the 120ROM and 60ROM protocols. After the protocols, we found greater total work (TW) for the 120ROM protocol (Table 1), due to the two-fold greater ROM performed at the ECC. We did not control for TW, as we wanted to investigate the effect of the same number of contractions and velocity, modulating only total ROM. Although the difference in TW could have an impact on the results, it may not be large, as it was demonstrated that TW performed at the ECC did not correlate

well with changes in any indirect muscle damage markers [20]. Chapman *et al.* [20] suggest that high variability in the changes in common markers of muscle damage after eccentric exercise could be explained by the variability in TW produced in the exercise. To test this hypothesis, 53 subjects were submitted to maximal 60 eccentric actions of the elbow flexors on an isokinetic dynamometer that forcibly extended the elbow joint from 60° to 180° at a constant velocity (90° s⁻¹). The results showed large variability of the total work between subjects (695 to 7702 J), but no association with the magnitude of changes in indirect markers of muscle damage. Therefore, we suggest that the major impact in our results was indeed due to the difference in total ROM.

The main comparisons in the present study demonstrated greater decreases in muscle strength (i.e., MVC-ISO) for the 120ROM protocol compared with the 60ROM protocol. Muscle strength is considered one of the most reliable indirect markers of muscle damage [21]. The decline in muscle force production in the days following ECC can vary from 9 to 50% [22-24]. This variation is related to variables such as exercise intensity [4], velocity of movement [5], and muscle exercise protocol [6, 7], which makes difficult the comparison of previous studies with the results presented herein. However, this variation in the decrease of muscle strength has been used to classify the magnitude of muscle damage in mild damage (no more than -20%), moderate damage (-20 to -50%) and severe damage (more than -50%) [25]. According to this classification, the 60ROM protocol showed mild damage (12-23% loss of strength), while the 120ROM protocol showed moderate damage (25-38% loss of strength). This difference can also be confirmed by greater effect size values for the 120ROM protocol (MVC-ISO, ES: 1.97) compared with the 60ROM protocol (MVC-ISO, ES: 0.93). As well as MVC-ISO, muscle soreness was greater for the 120ROM protocol (19 mm; ES: 1.18) compared with the 60ROM protocol (8 mm; ES: 1.07). It is suggested that the muscle tissue and the muscle-tendon junction have free nerve endings responsible for the mechanical and chemical information [26]. Thus, when the connective tissue surrounding the fibres is damaged by ECC, it becomes more sensitive to pain and produces decreases in ROM. This is evidenced in our study, as both protocols showed reduced ROM after the ECC protocols. Similarly as muscle soreness, reduces in ROM were greater for the 120ROM protocol (-11.5°; ES: 1.27) compared with the 60ROM protocol (4.1°; ES: 0.63). Overall, our results indicate clearly that a protocol with a two-fold greater ROM induces a higher degree of muscle damage than a smaller ROM, even when the protocols are performed to the same end-point of ROM.

The findings of the present study support the commonly held belief amongst athletes and coaches that a large ROM results in a higher level of muscular stress, which promotes greater muscle soreness and muscle damage. The prolonged deficit in strength and increase in muscle soreness following a large ROM in the untrained population used in this study may negatively affect the daily activities in this population. Therefore, practitioners should be careful with

exercises with large amplitudes in the early stages of training to avoid compromising adherence to exercise programmes.

CONCLUSIONS

In conclusion, ECC of the elbow flexors with a 120° ROM promotes a greater magnitude of muscle damage compared to an ECC protocol with a 60° ROM. This conclusion is highlighted by greater changes in all indirect markers of muscle damage measured (MVC-ISO, ROM and muscle soreness) for the 120ROM protocol compared with the 60ROM protocol.

Acknowledgements

the study was also supported by the São Paulo Research Foundation (FAPESP) grants (#2013/21218-4 to CAL; #2012/24499-1 and #2014/19594-0 to FD; #2011/22122-5 to TFS) and National Council for Scientific and Technological Development (CNPq) grant (AGF)

Conflict of interests: the authors declared no conflict of interests regarding the publication of this manuscript.

REFERENCES

- Chen TC, Nosaka K, Sacco P. Intensity of eccentric exercise, shift of optimum angle, and the magnitude of repeated-bout effect. *J Appl Physiol.* 2007;102(3):992-999.
- Clarkson PM, Hubal MJ. Exercise-induced muscle damage in humans. *Am J Phys. Med Rehabil.* 2002;81(11):S52-69.
- Clarkson PM, Nosaka K, Braun B. Muscle function after exercise-induced muscle damage and rapid adaptation. *Med Sci Sports Exerc.* 1992;24(5):512-520.
- Nosaka K, Newton M. Difference in the magnitude of muscle damage between maximal and submaximal eccentric loading. *J Strength Cond Res.* 2002;16(2): 202-208.
- Nogueira FRD, Conceição MS, Vechin FC, Mendes Jr. EM, Rodrigues GFC, Fazolin MA, Chacon-Mikahil MP, Libardi CA. The effect of eccentric contraction velocity on muscle damage: A review. *Isok Exer Sci.* 2013;21:1-9.
- Chen TC, Chen HL, Lin MJ, Wu CJ, Nosaka K. Muscle damage responses of the elbow flexors to four maximal eccentric exercise bouts performed every 4 weeks. *Eur Appl Physiol.* 2009;106(2):267-275.
- Nogueira FR, Libardi CA, Nosaka K, Vechin FC, Cavaglieri CR, Chacon-Mikahil MP. Comparison in responses to maximal eccentric exercise between elbow flexors and knee extensors of older adults. *J Sci Med Sport.* 2014;17(1):91-95.
- Brooks SV, Zerba E, Falukner JA. Injury to muscle fibres after single stretches of passive and maximally stimulate muscles in mice. *J Physiol.* 1995;488(2):459-469.
- Talbot JA, Morgan DL. The effects of stretch parameters on eccentric exercise-induced damage to toad skeletal muscle. *Journal of Muscle Research and Cell Motility.* 1998; 19(3):237-245.
- Nosaka K, Sakamoto K. Effect of elbow joint angle on the magnitude of muscle damage to the elbow flexors. *Med Sci Sports Exerc.* 2001;33(1):22-29.
- Nosaka K, Newton M, Sacco P, Chapman D, Lavender A. Partial protection against muscle damage by eccentric actions at short muscle lengths. *Med Sci Sports Exerc.* 2005;37(5):746-753.
- Vaczi M, Costa A, Racz L, Tihanyi J. Effects of consecutive eccentric training at different range of motion on muscle damage and recovery. *Acta Physiol Hung.* 2009;96(4):459-468.
- Chapman D, Newton M, McGuigan MR, Nosaka K. Effect of lengthening contraction velocity on muscle damage of the elbow flexors. *Med Sci Sports Exerc.* 2008;40(5):926-933.
- Nosaka K, Clarkson PM. Variability in serum creatine kinase response after eccentric exercise of the elbow flexors. *Int J Sports Med.* 1996;17(2):120-127.
- Nosaka K, Newton M, Sacco P. Delayed-onset muscle soreness does not reflect the magnitude of eccentric exercise-induced muscle damage. *Scand J Med Sci Sports.* 2002;12(6):337-346.
- Ugrinowitsch C, Fellingham GW, Ricard MD. Limitations of Ordinary Least Squares Models in Analyzing Repeated Measures Data. *Med Sci Sports Exerc.* 2004;36(12):2144-2148.
- Cohen J. *Statistical power analysis for the behavioral sciences.* 1988; Hillsdale, NJ: Lawrence Erlbaum.
- Yu JG, Thornell LE. Desmin and actin alterations in human muscles affected by delayed onset muscle soreness: a high resolution immunocytochemical study. *Hist. Cell Biol.* 2002;118(2):171-179.
- Shepstone TN, Tang JE, Dallaire S, Schuenke MD, Staron RS, Phillips SM. Short-term high- vs. low-velocity isokinetic lengthening training results in greater hypertrophy of the elbow flexors in young men. *J Appl Physiol.* 2005;98(5):1768-1776.
- Chapman D, Newton M, McGuigan MR, Nosaka K. Work and peak torque during eccentric exercise do not predict changes in markers of muscle damage. *Br J Sports Med.* 2008;42(7):585-591.
- Warren GL, Lowe DA, Armstrong RB. Measurement tools used in the study of eccentric contraction-induced injury. *Sport Med.* 1999;27(1):43-59.
- Bourgeois J, MacDougall D, MacDonald J, Tarnopolsky M. Naproxen does not alter indices of muscle damage in resistance-exercise trained men. *Med Sci Sports Exerc.* 1999;31(1):4-9.
- Lauritzen F, Paulsen G, Raastad T, Bergersen LH, Owe SG. Gross ultrastructural changes and necrotic fiber segments in elbow flexor muscles after maximal voluntary eccentric action in humans. *J Appl Physiol.* 2009;107(6):1923-1934.
- Paulsen G, Egner IM, Drange M, Langberg H, Benestad HB, Fjeld JG, Hallen J, Raastad T. A COX-2 inhibitor reduces muscle soreness, but does not influence recovery and adaptation after eccentric exercise. *Scand J Med Sci Sports.* 2010;20(1): e195-207.
- Paulsen G, Mikkelsen UR, Raastad T, Peake JM. Leucocytes, cytokines and satellite cells: what role do they play in muscle damage and regeneration following eccentric exercise? *Exer Imm Rev.* 2012;18:42-97.
- Jamurtas AZ, Theocharis V, Tofas T, Tsiokanos A, Yfanti C, Paschalis V, Koutedakis Y, Nosaka K. Comparison between leg and arm eccentric exercises of the same relative intensity on indices of muscle damage. *Eur Appl Physiol.* 2005;95:179-185.