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Response of males and females to high-force eccentric exercise

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It has previously been shown that females incur less muscle damage than males after strenuous exercise, but limited data are available for humans. To determine possible differences between the sexes in humans, the response to high-force eccentric exercise was examined in a large sample of women ($n = 83$) and men ($n = 82$). The participants performed a bout of eccentric exercise of the elbow flexors consisting of 70 maximal repetitions. Isometric strength, resting elbow angle and muscle soreness were measured before, immediately after (except soreness) and then daily for 7 days after exercise. There was a significant loss in strength among both groups (69% for women and 63% for men) ($P < 0.01$) immediately after exercise; at 168 h post-exercise, women still had a 27% strength loss and men had a 24% strength loss. No significant difference in strength loss or recovery rate was found between men and women. Soreness reached peak values 32–48 h post-exercise ($P < 0.01$), with no significant difference between men and women. Range of motion decreased significantly until 3 days after exercise (14.6° or 0.255 rad loss for women; 12.2° or 0.213 rad loss for men) ($P < 0.01$); at 168 h post-exercise, the women and men still showed a loss of 4.8° (0.084 rad) and 4.0° (0.07 rad), respectively. There was a significant interaction of sex × time ($P < 0.01$); a *post-hoc* test indicated that the women experienced a greater loss in range of motion at 72 h than men and this difference was maintained to 168 h post-exercise ($P < 0.01$). Thus, our results do not support the contention that women have a lower response to eccentric exercise than men.

Keywords: females, males, muscle damage, muscle function, muscle soreness, pain.

Introduction

Strenuous over-exertion exercise, especially involving unaccustomed eccentric contractions, results in damage to skeletal muscle (Smith, 1991; Clarkson *et al.*, 1992; Clarkson and Newham, 1995; MacIntyre *et al.*, 1995). Damage has been documented directly from analysis of biopsy samples and indirectly from losses in strength and range of motion and increases in muscle proteins (e.g. creatine kinase) in the blood. Creatine kinase is commonly assessed as an indicator of muscle damage, but there is a larger inter- and intra-participant variability in the increase of serum or plasma creatine kinase activity after exercise (Clarkson *et al.*, 1992; Clarkson and Newham, 1995; Nosaka and Clarkson, 1996). Despite the problem with creatine kinase as an indicator of damage, most studies that have examined differences between the sexes in response to eccentric exercise have assessed changes in creatine kinase; the results of these studies are equivocal.

Previous research on animals suggests that female muscle may be protected from exercise-induced damage, leading to the common belief that females show less muscle damage than males. These studies, which either examined differences between the sexes or manipulated oestrogen levels, found that females may be more resistant to the damaging effects of exercise, perhaps as a consequence of oestrogen (Amelink and Bär, 1986; Amelink *et al.*, 1988, 1990; Bär *et al.*, 1988; Koot *et al.*, 1991; Van der Meulen *et al.*, 1991). However, two studies that examined morphological changes in male and female rats after eccentric exercise reported conflicting results. Van der Meulen *et al.*

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(1991) found no significant difference in morphological changes between male and females, whereas Amelink *et al.* (1991) observed more damage in male rats after exercise.

Some early research in humans also led to the contention that women incur less muscle damage. Resting serum creatine kinase was found to be lower in women than men, and women showed a lower serum creatine kinase response to an aerobic or endurance exercise regimen (Brooke *et al.*, 1979; Shumate *et al.*, 1979; Bär *et al.*, 1985; Norton *et al.*, 1985; Apple *et al.*, 1987; Harris *et al.*, 1991). These exercise regimens, however, produced little muscle damage compared with high-force eccentric exercise regimens. In a preliminary study that examined serum creatine kinase activity in women and men who performed maximal eccentric actions of the forearm flexor muscles – an exercise well-documented to produce substantial muscle damage (Clarkson *et al.*, 1992) – Miles *et al.* (1994) found that women demonstrated a greater peak and relative increase in serum creatine kinase after exercise than men. The same patterns were found when the contralateral limb was exercised 21 days later.

The results suggesting that women incur less muscle damage after exercise than men are based on inappropriate exercise tests, the use of a highly variable indicator of damage, and small sample sizes. No published studies have evaluated changes in muscle function in response to an exercise damage protocol in women and men. Maximal voluntary force production and range of motion provide less variable and more reliable methods for assessing exercise-induced muscle injury than serum creatine kinase activity (Clarkson *et al.*, 1992; Warren *et al.*, 1999). In the present study, we compared changes in muscle force production, angle about the elbow as an indicator of range of motion, and muscle soreness sensation in a large sample of women and men after high-force eccentric exercise to determine whether differences between the sexes exist in these muscle function assessments.

Methods

Participants

The work reported here was part of a larger double-blind study to assess the effects of a muscle analgesic on muscle pain induced by exercise. Here, only data from the placebo group are analysed; the remaining results are unpublished. The study was undertaken at two sites – Chicago, IL and Amherst, MA – using exactly the same protocols. Altogether, 406 men and 396 women entered the study, of whom 259 men (64%) and 255 women (64%) reported at least moderate soreness. If participants did not report such soreness, they were excluded from the study. We did not include participants who did not report moderate soreness because the primary intention of the original study was to assess the effectiveness of an analgesic on muscle soreness. However, it is important to note that the proportion not reporting moderate soreness (64%) was the same for men and women. Eighty-two men and 83 women were placed at random in the placebo group. Although menstrual cycle was not controlled for, we do not believe that this would be a major confounding factor for two reasons. First, in a previous study in our laboratory, we did not find differences in the exercise-induced damage response when participants were exercised in the follicular and luteal phases of the cycle (McCormick *et al.*, 1985). Secondly, the difference in oestrogen between men and women would be considerably greater than any difference over the cycle in women.

Protocol

The participants visited the laboratory on nine occasions, the last eight of which (visits 2–9) were on consecutive days. On the first visit (visit 1), participants gave written informed consent and were screened to ensure that no strength or resistance exercise had been performed in the previous year. The informed consent and the study protocol were approved by the university's Human Subjects Review Committee. A complete medical history and physical examination were completed by a licensed physician. The physician also established that the participants were not taking any medication that might interfere with their rating of soreness. Baseline measures of soreness, relaxed arm angle and maximal isometric strength were taken. The first visit was scheduled no more than 1 week before the second.

On the second visit, baseline measures of soreness, relaxed arm angle and maximal isometric strength were again recorded; they were not to exceed $\pm 10\%$ of the mean at the first visit. This was to ensure consistency of the performance measures. If participants recorded a more than 10% difference between visit 1 and visit 2, they were excluded from the study. Immediately after recording the baseline measures, the participants completed the exercise protocol, after which post-exercise measures of relaxed arm angle and maximal isometric strength were again recorded.

Visit 3 was scheduled 1 day after visit 2, within ± 1 h. During visit 3, soreness, relaxed arm angle and maximal isometric strength were again assessed. This time, the participants were assigned at random to one of four treatment groups (double-blind). Only the results for participants randomized into the placebo group (82 men, 83 women) are considered here. The age, height and body mass of the female participants were 24.8 ± 4.9 years, 164 ± 8 cm and 66.3 ± 14.6 kg (mean ± *s*), respectively; those of the male participants were 24.7 ± 5.1 years, 180 ± 8 cm and 78.7 ± 14.3 kg, respectively.

Identical procedures were followed for visits 4–9; soreness was assessed first, followed by relaxed arm angle and maximal isometric strength. Soreness was also assessed 32 h post-exercise.

Criterion measure assessment

Muscle soreness was assessed using two different procedures. Soreness upon lifting of the exercised elbow flexor muscles was assessed subjectively by the participant using a 100 mm visual analog scale, with 'no soreness' (0 mm) and 'severe soreness' (100 mm) serving as the left and right anchors, respectively. The participants reported soreness upon lifting a one pound (0.45 kg) weight three times, having been instructed to go through the entire range of motion about the elbow. Soreness upon palpation of the exercised elbow flexor muscles was assessed using an identical 100 mm visual analog scale. The participants gently palpated their elbow flexor muscles and rated their soreness on the basis of the feeling of the sorest aspect.

Relaxed arm angle was recorded after marking three anatomical landmarks with permanent non-erasable ink on the exercised arm to ensure consistent measurement over days. The acromion process of the scapula, lateral epicondyle of the humerus and styloid process of the radius were the landmarks used, and measurements were taken using a long-arm mechanical (self-constructed) goniometer aligned over these reference points. Relaxed arm angle was measured with the participants facing straight ahead with their exercised arm fully relaxed and hanging by their side. Measures were performed in triplicate and the mean value was used in the subsequent analysis.

Maximal isometric force production of the exercise elbow flexor muscles was assessed with the elbow positioned at an angle of 90° (1.57 rad), determined by goniometry. Maximal isometric force production was tested in a preacher curl machine identical in dimensions to the one used for the exercise. A strain gauge (model 32528CTL, Lafayette Instrument Company, Lafayette, IN) connected the base of the machine and the forearm lever arm. The mean of three maximal 3 s trials separated by 1 min rest was recorded for subsequent analysis.

Exercise regimen

For the eccentric exercise regimen of the elbow flexor muscles, the participants were seated in a modified preacher bench machine, two cushions holding the arm in place. The arm was in turn connected to a lever arm, which the investigator held (Clarkson *et al.*, 1992). The participants were instructed to resist the downward force applied by the investigator and begin pulling upwards when the investigator moved the lever arm to its uppermost position and gave a verbal cue. The participants were verbally encouraged to produce maximal resistance throughout the entire range of motion while the investigator lowered the lever arm. Because of the mechanical advantage of the lever system, the investigator could easily resist and overcome the force that both female and male participants produced, ensuring maximal resistance for all participants. The amount of strength loss and the amount of loss in arm angle immediately after exercise was 63% and 9.3° (0.163 rad) respectively for men, and 69% and 6.7° (0.117 rad) respectively for women. These similar responses to the exercise by men and women indicated that they were similarly stressed by the exercise. The participants started the movement with the arm in a fully flexed position and ended with it in a fully extended position. Each eccentric action took 3 s to complete, and contractions were repeated every 15 s. A total of 70 maximal contractions were completed, with a 5 min break midway through the exercise protocol.

Statistical analyses

The baseline data were analysed first to assess stability (repeated-measures analysis of variance) and reliability (intraclass R) of the strength and arm angle measurements. There was no significant difference between the baseline days for the strength and arm angle measures and no significant interaction of sex × time. The correlation coefficients were $R = 0.97$ and $R = 0.90$ for strength and arm angle, respectively. Thus, the reliability of the measures was judged to be high. The measurements taken directly before exercise on the second baseline day were used for further analysis. These data were analysed with a two-factor (2 × 9, sex × time) repeated-measures analysis of variance. In the case of a significant interaction term, a repeated-measures analysis of variance was used as a *post-hoc* test to determine if the significance was due to a greater decrement in function or to an impaired rate of recovery in one group compared with the other. Furthermore, a Tukey's *post-hoc* test was used to detect specific differences between time points. Significance was set at $P < 0.05$.

Results

Figures 1 and 2 present the changes in soreness with palpation and with lifting, respectively. Significant

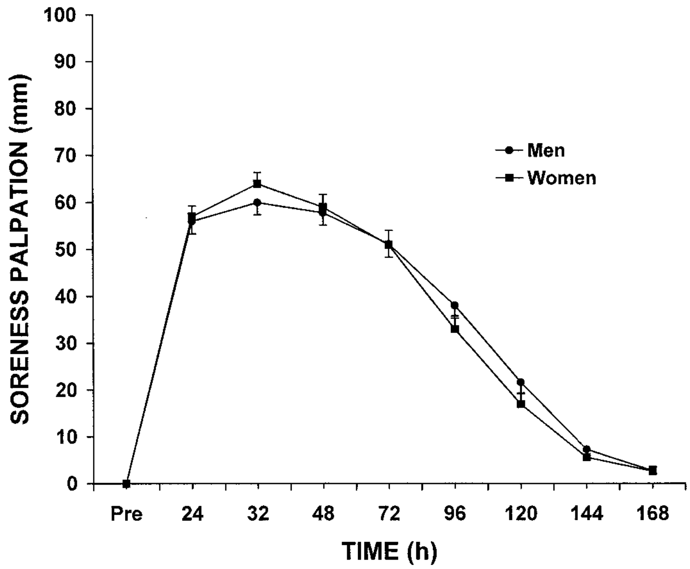

Fig. 1. Muscle soreness with palpation assessed pre-exercise (0 h) and up to 168 h post-exercise (mean ± standard error).

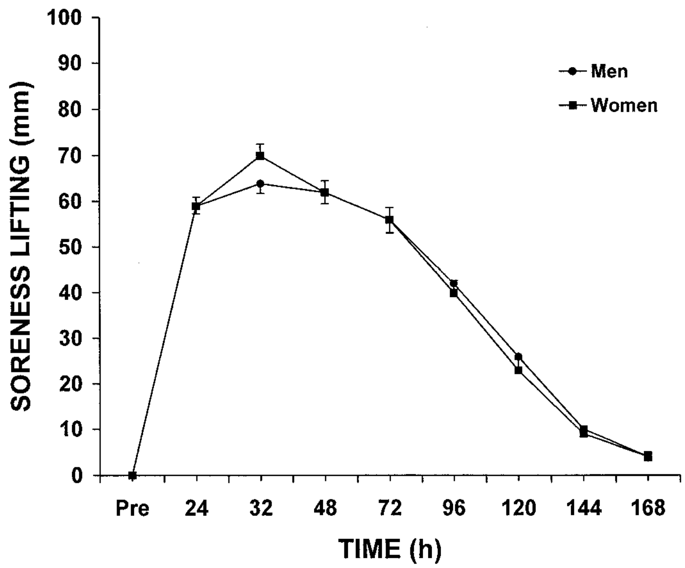

Fig. 2. Muscle soreness while lifting a low load weight assessed pre-exercise (0 h) and up to 168 h post-exercise (mean ± standard error).

soreness developed (main effect of time: soreness upon palpation, $F_{8,1304} = 463$, $P < 0.01$; soreness upon lifting, $F_{8,1304} = 547$, $P < 0.01$) and peaked at approximately 32–48 h post-exercise for both groups. There was no significant difference between men and women (main effect of group: soreness upon palpation, $F_{1,163} = 0.06$, $P = 0.80$; soreness upon lifting, $F_{1,163} = 0.001$, $P = 0.97$). There was no significant interaction between sex and time for either measure ($F_{8,1304} = 1.43$, $P = 0.18$ and $F_{8,1304} = 1.06$, $P = 0.39$, respectively).

Strength as a percentage of change from baseline is shown in Fig. 3. The baseline absolute mean ± standard deviation was 70.8 ± 16.5 kg and 37.3 ± 10.8 kg for the men and women, respectively. There was a significant loss in strength after exercise that was not fully restored 7 days post-exercise (main effect of time: $F_{8,1304} = 430$, $P < 0.01$). Over time, there was no significant difference between groups ($F_{1,163} = 2.4$, $P = 0.12$) and the interaction of sex and time ($F_{8,1304} = 1.05$, $P = 0.39$) was non-significant. Men and women experienced the same loss in relative strength after the eccentric exercise protocol, and the recovery of strength was the same.

The relaxed arm angle results are presented in Fig. 4. There was a significant loss in range of motion in the

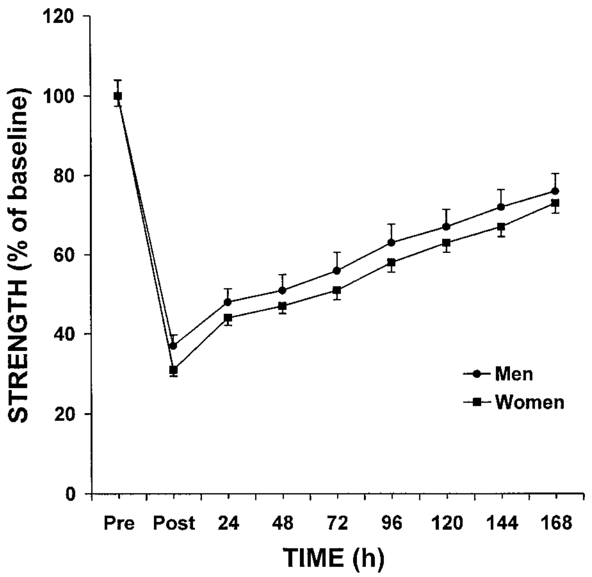

Fig. 3. The percentage loss in isometric strength immediately post-exercise (Post) and up to 168 h post-exercise (mean ± standard error).

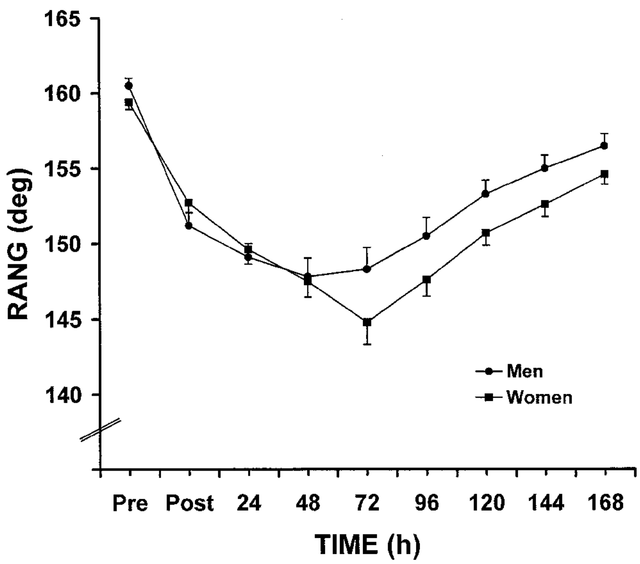

Fig. 4. Relaxed arm angle (RANG) assessed pre-exercise (Pre), immediately post-exercise (Post) and up to 168 h post-exercise (mean ± standard error).

first 3 days post-exercise, which was not fully restored by 7 days post-exercise (main effect of time: $F_{8,1304} = 89.8$, $P < 0.01$). There was no significant difference between groups (main effect of group: $F_{1,163} = 1.7$, $P = 0.20$), but there was a significant interaction term, indicating that overall the pattern of response differed between men and women ($F_{8,1304} = 3.63$, $P < 0.01$). To determine whether the interaction term reflected a faster recovery rate, the data were analysed to assess the difference over time between 72 and 168 h. There was a significant main effect of group ($F_{1,163} = 4.97$, $P < 0.05$), but no significant interaction term; this indicated that, although the men showed a smaller loss in range of motion, the rate of recovery was the same between groups. When a Tukey *post-hoc* test was calculated, we found that the men and women did not differ in loss of range of motion up to 48 h post-exercise. However, at 72 h there was a significant difference between men and women, which was maintained until 168 h post-exercise ($P < 0.05$).

Discussion

In this study, we found that after unaccustomed high-force eccentric exercise, which is known to result in muscle damage, men and women showed a similar loss and recovery of isometric strength. They also exhibited a similar development of reported intensity of soreness and dissipation of soreness. Although there was a significant difference in the pattern of response between men and women for range of motion, the women actually showed more pronounced, albeit small, changes.

Most previous research that assessed possible differences between the sexes in response to damage-inducing exercise concentrated on the measurement of enzyme release from muscle, especially creatine kinase, as an indirect marker of tissue damage. Human studies have found that women exhibit a lower serum creatine kinase response to an aerobic exercise regimen (Brooke *et al.*, 1979; Shumate *et al.*, 1979). In marked contrast, Miles *et al.* (1994) examined the creatine kinase response of non-weight-trained women and men who performed 50 maximal eccentric actions of the forearm flexor muscles. They found that the women had a lower baseline creatine kinase concentration (80 $U \cdot l^{-1}$) than men (139 $U \cdot l^{-1}$), but the women exhibited a greater peak and relative increase in serum creatine kinase in response to the high-force eccentric exercise. Why women may have a lower creatine kinase response to an aerobic-type exercise than men, whereas they do not have a lower response to a high-force eccentric exercise, is not known. However, oestrogen may play a protective role as an antioxidant and membrane stabilizer during exercise with a relatively high oxidative stress (Clarkson and Sayers, 1999; Tiidus, 1999).

Although creatine kinase is used as an indirect marker of muscle damage, there is a larger inter- and intra-participant variability in the creatine kinase response after exercise because blood concentrations reflect what is being released from the damaged tissue as well as what is taken up by the reticuloendothelial system (see Clarkson *et al.*, 1992; Clarkson and Newham, 1995). In a recent study, Gunst *et al.* (1998) showed that serum creatine kinase activity was related to serum glutathione activity; they suggested that glutathione served as a creatine kinase-preserving agent during the lifetime of the enzyme in the circulation. Thus, blood creatine kinase concentrations provide an indirect qualitative marker of muscle damage and may be influenced by factors other than damage.

Currently, no data exist on direct measures of muscle damage between human males and females, and the results from animal studies are equivocal. A few studies of morphological assessment of animal muscle after damage-inducing exercise have been performed, but they all used aerobic-type exercise. For example, Komulainen *et al.* (1999) recently found that female rats showed a slower development of damage and less marked damage in histological analysis of muscle than male rats after downhill running for 130 min.

A more reliable assessment of exercise damage than blood creatine kinase is isometric strength (Warren *et al.*, 1999). We found no difference in the relative strength loss immediately after exercise or in the rate of strength recovery between men and women. In a study of mouse muscle, Warren *et al.* (1996) examined the effect of electrically stimulated eccentric contractions in ovariectomized mice administered oestradiol or an inert oil for the previous 21 days. The decrement in force after the eccentric contractions was similar between groups, although the oestradiol group appeared to suffer a greater loss in force-generating ability.

Several studies have suggested an analgesic effect related to oestrogen. Thompson *et al.* (1997) found that when women taking oral contraceptives were exposed to nearly constant amounts of oestrogen and progesterone, they reported significantly less soreness than eumenorrhoeic controls. Thompson *et al.* suggested that peripheral sex steroids may modulate pain perception through the endogenous opiate system. Gintzler and Bohan (1990) and Dawson Basoa and Gintzler (1998) reported that the pain threshold was increased in both animals and humans during gestation, possibly due to an alteration in the peripheral sex steroids. Female rats were found to possess a spinal analgesic system that could be positively modulated by circulating sex steroids (Dawson Basoa and Gintzler, 1996). In animal models, cyclic changes in the oestrous cycle affected pain perception such that pain was reduced in the presence of increased oestrogen (Martínez Gómez *et al.*, 1994). Even though we did not control for the menstrual cycle in the women tested, the amount of circulating oestrogen, even at the lowest point in the cycle, would still be greater than in men.

In contrast to the above results, several authors have reported an increase in pain perception associated with oestrogen. Ellermeier and Westphal (1995) found that women reported greater pain and greater pupil dilation in response to a pressure-induced pain test, but only when high pressures were used. Generally, women experience greater sensitivity to noxious stimuli than men (Fillingim *et al.*, 1998). Muscular skeletal pain has been found to be more common among women (Rajala *et al.*, 1995). In a recent study, women experienced more pain than men after a jaw-clenching exercise (Plesh *et al.*, 1998).

Our results differ from those of previous studies in that there was no difference in pain perception after eccentric exercise. It should be noted that most other studies used small sample sizes, commonly 10 participants or less per group (Ellermeier and Westphal, 1995; Thompson *et al.*, 1997; Plesh *et al.*, 1998), which may not have the statistical power to discriminate subjective measurements that have a high subjectivity and variability in their response. Also, the means to elicit pain and type of pain have differed between studies. Muscle soreness or pain after strenuous exercise has a characteristic and unique pattern of development, with a delayed peak of about 30 h post-insult. Moreover, this soreness is predominantly perceived upon movement. These characteristics differ from an acute (sharp) pain or a constant ache, and make it difficult to compare our results with those of studies of differences between the sexes in terms of acute, experimental pain perception. However, the 82 men and 83 women in the present study clearly showed a similar response in terms of delayed onset pain or soreness after eccentric exercise of the elbow flexor muscles.

The women in the present study experienced a slightly greater loss in range of motion than the men: the cause of this difference is unclear. Moreover, the mechanism driving the well-documented decrease in range of motion is not known (Clarkson *et al.*, 1992; Clarkson and Newham, 1995). One proposed theory is that the muscle shortening is due to a shortening or reconfiguration of connective tissue (Jones *et al.*, 1987). Connective tissue diseases are more common in women (Lahita, 1996a,b), suggesting that there is perhaps a difference between the sexes in the property of connective tissue. Thus, if connective tissue is more susceptible to injury in women, this may have contributed to the more pronounced muscle shortening and reduction in the elbow angle. However, it should be noted that the difference in loss of range of motion between men and women was small.

In summary, men and women developed similar muscle soreness and demonstrated similar relative strength loss and recovery over time. The loss of range of motion was the same for women and men over the first 48 h post-exercise. However, for the women, the loss in range of motion continued; at 72 h, the women experienced a significantly greater loss of range of motion than men. This difference was maintained up to 168 h post-exercise. Thus, the results of the present study do not support the contention that women experience less muscle damage in response to maximal high-force eccentric exercise using muscle function assessment and soreness evaluation. Moreover, for the range of motion assessment, women appeared to be more severely affected by the exercise.

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