

Differences in muscle pain and plasma creatine kinase activity after 'up' and 'down' Comrades marathons

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Abstract

Objective. The aim of this study was to compare the acute changes in muscle pain and plasma creatine kinase (CK) activity following the 'up' and 'down' Comrades marathon.

Design. This was a quasi-experimental design. Eleven male runners (39.7±9.3 years) completed the 'up' Comrades marathon, and 11 male runners (41.0±8.4 years) completed the 'down' Comrades marathon the following year. Maximum oxygen consumption and peak treadmill running speed were measured 2 weeks before the race. Daily measurements of muscle pain and plasma creatine kinase (CK) activity were recorded 1 day before, and for 7 days after the race.

Results. Muscle pain remained significantly elevated for up to 7 days after the Comrades marathon, compared with pre-race values ($p<0.0009$). The pain scores following the 'down' run were significantly higher than the pain scores following the 'up' run for at least 7 days after the race ($p<0.004$). Plasma CK activity re-

mained significantly elevated for up to 5 days after the Comrades marathon, compared with pre-race values ($p<0.007$). Plasma CK activity following the 'down' run was significantly higher than the plasma CK activity following the 'up' run for 5 days after the race ($p<0.04$). A high degree of intra-individual variability in plasma CK activity was observed.

Conclusions. The 'down' Comrades marathon causes significantly more muscle pain and plasma CK activity compared with the 'up' Comrades marathon. Further studies are required to accurately define the regeneration of muscle following the Comrades marathon.

Introduction

The Comrades marathon is a 90 km ultramarathon race, run annually between Durban and Pietermaritzburg, South Africa. However, the start and finish of the race alternate each year, and the race is therefore run in different directions. In the 'up' run the race starts at sea level in Durban, and runners ascend to the finish in Pietermaritzburg, at 650 m above sea level. The highest point in the race is 870 m above sea level. In the 'down' run, the race starts in Pietermaritzburg, and runners descend to the finish in Durban.¹¹

Marathon and ultramarathon races impose severe physiological stresses on runners.^{6,17} Previous studies on runners of the 90 km Comrades marathon have provided information regarding changes in ECG activity,¹³ serum enzyme activities, fluid balance,¹² renal function,¹⁹ factors explaining the development of hyponatraemic encephalopathy,¹⁸ and the decrement in muscle power associated with muscle damage.⁶

It is well documented that muscle damage is a common occurrence associated with distance running.^{6,17} Exercise-induced muscle damage is characterised by a disruption of the sarcolemma,² sarcotubular system,^{2,4} contractile components of the myofibril, the extracellular matrix and the cytoskeleton.¹⁵ Distance running is

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also associated with impaired muscle function,^{6,23,24} and delayed-onset muscle soreness (DOMS).²² Previous studies have shown that muscle pain associated with DOMS usually dissipates within 96 hours after exercise,^{3,5} but may persist for up to 10 days after exercise.⁸

Plasma creatine kinase (CK) activity is one of the most commonly used indicators of muscle damage.²² Creatine kinase is released into the blood when the cell membrane is damaged, or when there is an alteration in cell membrane permeability.¹ The extent and duration of the plasma CK response to exercise varies according to the type of exercise.⁷ Plasma CK activity peaks within 24 - 48 hours after a marathon.^{22,27}

Anecdotally, runners report a greater degree of muscle pain and a prolonged recovery period following the 'down' run, compared with the 'up' run. This is not unexpected, as during the 'down' run there will be more eccentric strain on the muscles, which is known to be a risk factor for causing muscle damage.⁹ However, the anecdotal observations have not been confirmed experimentally and the physiological responses associated with DOMS following the Comrades marathon have not been established.

Accordingly, the aim of this study was to compare acute changes in muscle pain and plasma creatine kinase activity following the 'up' and 'down' Comrades marathon.

Methods

Subjects and study design

Twenty-two healthy male runners who participated in the Comrades marathon were selected for the study, which had a quasi-experimental design. The study was granted ethical clearance by the Ethics and Research Committee of the Faculty of Health Sciences, University of Cape Town. Subjects gave written consent after being informed about the demands of the study. The subjects completed a questionnaire to determine their age, training history, medical and surgical history, and any past or present injuries to the lower limbs.

The study was conducted over a 2-year period. Eleven subjects participated in the 'up' Comrades marathon, and 11 subjects participated in the 'down' Comrades marathon. One subject participated in both the 'up' and 'down' races. The subjects were requested to avoid any medication, and strenuous training and racing, other than the Comrades marathon, for the duration of the study (± 20 days). Testing occurred at a similar time (to within 1 hour) for each subject for the duration of the study.

Preliminary testing

Preliminary testing was conducted on all subjects 2 weeks before the Comrades marathon. All subjects had their body composition assessed. Body fat was represented as the sum of seven skinfolds (biceps, triceps, subscapular, supra-iliac, calf, thigh and abdomen), as described by Ross and Marfell-Jones,²⁹ and also as a percentage of body mass.¹⁴

A maximal treadmill test was performed to determine maximum oxygen consumption (VO_{2max}), peak treadmill running speed (PTRS), and maximum heart rate (HR_{max}). The maximal test was performed on a treadmill (Quinton Instruments, Seattle, WA, USA) with the elevation set at 1%, in order to reproduce the energetic cost of running outdoors on a flat surface.²⁰

The subjects warmed up before the maximal test. The timing and intensity of the warm-up was specific for each subject, and was maintained for the duration of the study. The test began with the treadmill speed set to $10 \text{ km}\cdot\text{h}^{-1}$. This speed was maintained for 2 minutes, after which it was increased by $0.5 \text{ km}\cdot\text{h}^{-1}$ every 30 seconds until the subjects were unable to maintain the speed of the treadmill. During the maximal test, subjects wore a mouthpiece and a nose clip.

The expired air passed through an online computer system attached to an Oxycon Alpha automated gas analyser (Jaeger/Mijnhardt, Groningen, The Netherlands) for the determination of oxygen consumption (VO_2) and respiratory exchange ratio (RER). Before each test, the gas analyser was calibrated with a 3 L Hans Rudolph 5530 L syringe and an online $CO_2:N_2$ gas mixture of known composition. Heart rate was recorded (Polar Vantage XL, Polar Electro, Kempele, Finland) at 5-second intervals. VO_{2max} was defined as the VO_2 value that coincided with volitional fatigue. PTRS was defined as the highest speed that the runner could maintain for a complete 30-second increment prior to fatigue. HR_{max} was recorded as the highest heart rate during the last 30 seconds of the treadmill test.

Muscle pain

Muscle pain was measured daily for 1 day before, and for 7 days after the Comrades marathon. Muscle pain was measured subjectively, where subjects rated lower limb pain according to a 'rating of perceived pain' on a scale of 0 to 10, where 0 represents 'no pain', and 10 represents 'maximal pain'. This method of measurement of muscle pain has previously been shown to be highly correlated with objective pain measures.³⁰

Plasma creatine kinase activity

Daily blood samples, for the analysis of plasma creatine kinase (CK) activity, were collected for 1 day before, and for 7 days after the Comrades marathon. A 5 ml blood sample was taken from the subject's antecubital vein for the analysis of plasma CK activity. The blood samples were collected into pre-chilled tubes containing lithium heparin and were kept on ice for a maximum of 3 hours until centrifugation.

Blood samples were centrifuged at $2000 \times g$ for 10 minutes at 4°C , and plasma was stored at -20°C until the analysis of plasma CK activity. Plasma CK activity was measured by spectrophotometric (Beckman Instruments, Fullerton, CA) enzymatic assays (CK-NAC activated, Boehringer Mannheim Automated Analysis for BM/Hitachi Systems 704, Meylan, France).

Comrades marathon

The Comrades marathon race profiles for the 86.55 km 'up' run, and the 89.9 km 'down' run are shown in Fig. 1(a) and 1(b) respectively.¹¹ Comrades race speed was expressed as a percentage of each subject's personal best 10 km speed.

Statistical analyses

Statistical analyses were performed using Statistica software (Stat-Soft, Inc. (2007) STATISTICA (data analysis software system), version 8.0. www.statsoft.com). Differences in descriptive variables between groups were assessed using an independent *t*-test. A Mann-Whitney U test was used to assess differences in the pain scores on each day between groups. A Friedman's ANOVA and Kendall's concordance were used to assess differences in the pain scores within groups over time. As the plasma CK activity data had unequal variance, the logarithm of each value was determined, and these values were then used in an analysis of variance (ANOVA) with repeated measures to determine the significance for the two main effects of group and time, and the interaction (group \times time). A Tukey's *post hoc* test was used to identify specific differences. All data are presented as the mean \pm standard deviation. Statistical significance was accepted as $p < 0.05$.

Results

The descriptive characteristics of subjects are shown in Table I, and the training and racing history of subjects are shown in Table II. There were no significant differences between groups for any

of the descriptive variables. There were significant differences in the 10 km personal best times ($p < 0.006$) and the 42 km personal best times ($p < 0.04$) between groups, with the 'down' group being significantly faster over both distances. However, when the Comrades race speeds were expressed as a percentage of the subjects' 10 km personal best speed there were no differences between groups. There were no significant differences between groups for any of the other training history variables.

The subjects in the 'up' group completed the 86.55 km race in 606.6±39.2 minutes. The average intensity (% HR_{max}) during the race was 83.5±4.0%. The subjects in the 'down' group completed the 89.9 km race in 566.4±64.5 minutes. The average intensity (% HR_{max}) during the race was 79.2±2.2%. There were no differences between groups in race time or intensity.

Muscle pain

The muscle pain of subjects in the 'down' and 'up' groups is shown in Fig. 2. The subjective pain scores (arbitrary units) were significantly higher in the 'down' group on days 1 (6.6±2.0 v. 4.2±0.8; $p < 0.004$), 2 (6.2±1.9 v. 2.8±.1; $p < 0.0003$), 3 (5.3±1.4 v. 2.1±1.4; $p < 0.0004$), 4 (4.3±1.2 v. 1.3±1.3; $p < 0.0005$), 5 (3.6±1.3 v. 0.7±0.9; $p < 0.0003$), 6 (3.0±1.3 v. 0.6±0.9; $p < 0.0008$), and 7 (2.6±1.1 v. 0.4±0.7; $p < 0.0004$) after the Comrades marathon, compared with 'up' group values on the same days. Although muscle pain in the 'up' group had returned to pre-race values by day 7 after the Comrades marathon, muscle pain in the 'down' group remained elevated compared with pre-race values (2.6±1.1 v. 0.0; $p < 0.0009$).

Plasma CK activity

There was a significant interaction between groups over time for plasma CK activity ($F_{(7, 140)} = 3.13$; $p < 0.004$) (Fig. 3). Plasma CK activity was significantly higher in the 'down' group on days 1, 2, 3, 4, and 5, compared with pre-race values ($p < 0.007$). Plasma CK activity was also significantly higher in the 'up' group on days 1, 2, and 3, compared with pre-race values ($p < 0.006$). Plasma CK activity had therefore returned to pre-race values by day 4 in the 'up' group, and day 6 in the 'down' group. Other differences between days and groups are shown in Fig. 3.

Discussion

The Comrades marathon induced muscle pain in both groups consistent with delayed-onset muscle soreness (DOMS).⁷ The onset of muscle pain in both groups occurred within the first 24 hours following the race, which is consistent with other studies investigating the onset of DOMS resulting from exercise-induced muscle damage.^{8,25} In the 'up' group, subjective pain had returned to pre-race values by day 5 after the race. However, in the 'down' group, muscle pain remained elevated at 7 days after the race. Studies have shown that muscle pain associated with DOMS usually dissipates within 96 hours after exercise,^{3,5,10} but in some cases may persist for up to 10 days, particularly following high-force eccentric exercise protocols involving maximal contraction of the elbow flexors.⁸ Unfortunately data were not collected beyond 7 days, therefore the exact time course of recovery of muscle pain following the 'down' run is unclear.

Further, although the time course of recovery of muscle pain is similar following different types of exercise-induced muscle damage, the extent of soreness may vary. For example, high-force eccentric exercise protocols involving maximal contraction of the elbow flexors are associated with higher subjective pain scores compared with protocols involving downhill running.⁷

This is the first study to demonstrate a difference in subjective pain scores following the 'up' compared with the 'down' Comrades marathons. It is logical to assume that the difference in pain scores between the 'down' and 'up' groups is related to the increased amount

of downhill running during the 'down' Comrades marathon. Downhill running is associated with a greater magnitude of eccentric (muscle-lengthening) action compared with level running, and therefore a greater degree of muscle damage.³

The underlying mechanisms for the pain associated with DOMS are not well understood. It has been suggested that soreness may result from swelling and pressure in the muscle.³¹ Although biopsy studies have demonstrated increases in muscle fibre area and intramuscular pressure,¹⁶ discrepancies between the timing of peak muscle soreness and oedema have been identified.²⁶

It has also been suggested that chemicals such as histamines, prostaglandins, and bradykinins may be associated with the development of muscle soreness following exercise-induced muscle damage. It is theorised that these substances are released when the muscle is damaged, resulting in activation of type III and IV nerve afferents, leading to the sensation of pain.²⁸ However, there is no direct evidence to support this theory.⁷

In addition, although subjective pain remained significantly elevated for up to 7 days after the Comrades marathon, this does not necessarily reflect the magnitude of muscle damage⁵ or long-term changes in neuromuscular function. For example, it is known that neuromuscular function is disturbed for at least 11 days after the Comrades marathon.⁶ Furthermore, signs of regeneration are still present in the muscle of runners 12 weeks after a standard marathon, despite the absence of pain.³² There is a complex interaction between exercise-induced muscle damage and fatigue due to prolonged exercise. This is characterised by alterations in neuromuscular function including an increase in contact time, decreases in stretch reflex sensitivity, preactivation, and elastic energy potential, and changes in stiffness regulation.²¹ These factors are all affected by absolute running speed. It is acknowledged that a potential limitation of this study is the difference in 10 km personal best time between the 'up' and 'down' groups. Due to the inherent differences in distance and profile between the 'up' and 'down' runs, race speed was expressed as a percentage of the individual 10 km personal best time. Although no significant differences were observed in race

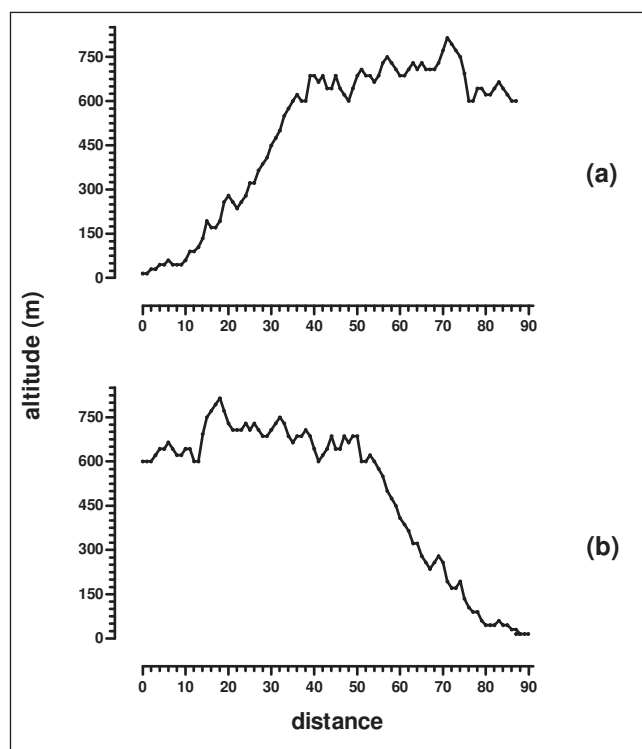


Fig. 1. Race profiles of the (a) 'up' and (b) 'down' Comrades marathon.

TABLE I. Descriptive characteristics of subjects in the 'up' (N=11) and 'down' (N=11) groups (mean ± SD)

Variable	Up	Down
Age (years)	39.7±9.3	41.0 ±8.4
Body mass (kg)	74.9± 4.6	71.8±11.6
Height (cm)	177.5±7.6	177.2±6.2
Sum of skinfolds (mm)	95.9±36.0	74.9±20.9
Body fat (%)	21.6±5.1	19.6±4.4
Maximum heart rate (b.min ⁻¹)	177±11	180±15
VO _{2max} (mlO ₂ .kg ⁻¹ .min ⁻¹)	54.7±7.2	57.8±5.5
Peak treadmill running speed (PTRS) (km.h ⁻¹)	16.7±1.5	17.6±1.7

TABLE II. Training and racing history of subjects in the up (N=11) and down (N=11) groups (mean ± SD)

Variable	Up	Down
Total years running	7.6±7.6	10.5±7.2
Pre-competition training distance (km.wk ⁻¹)	70.5±10.6	72.7±15.6
Average training distance (km.wk ⁻¹)*	56.6±6.5	55.5±11.7
Number of standard marathons (42 km)	30±30	37±26
Personal best 10 km time (min) [†]	43.1±3.0	37.9±3.3
Personal best 42 km time (min) [‡]	209.2±15.8	189.7±23.1
Race speed (%) [§]	60.1±3.5	60.7±5.8

* Average training distance in the 6 months preceding the race.
 † Significant differences:
 † Personal best 10 km time: up v. down (p<0.006)
 ‡ Personal best 42 km time: up v. down (p<0.04)
 § Comrades speed expressed as a percentage of 0 km personal best speed.

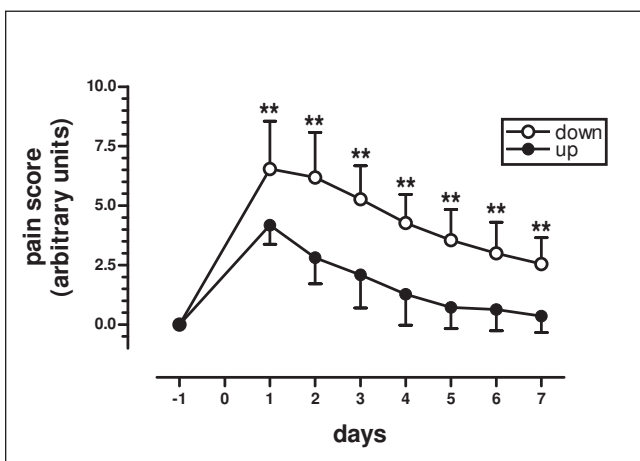


Fig. 2. Muscle pain (arbitrary units) of subjects in the 'up' (-●-) (N=11) and 'down' (-○-) (N=11) groups. Tests were conducted 1 day before the race, and daily for 7 days after the race. Data are expressed as mean ± SD. Significant differences: ** 'down' days 1, 2, 3, 4, 5, 6, and 7 v. 'up' days 1, 2, 3, 4, 5, 6, and 7 respectively (p<0.004).

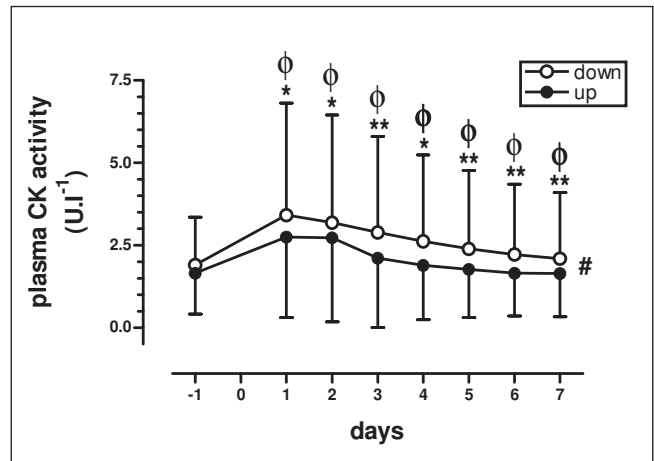


Fig. 3. Plasma creatine kinase activity (U.l⁻¹) of subjects in the 'down' (-○-) (N=11) and 'up' (-●-) (N=11) groups. Tests were conducted 1 day before the race, and daily for 7 days after the race. Data are expressed as mean ± SD.

Significant differences:

- ** 'down' day 1 v. 'down' days -1, 1, 3, 4, 5, 6, 7 (p<0.00003), and 2 (p<0.03)
- ** 'down' day 2 v. 'down' days -1, 4, 5, 6, and 7 (p<0.00003)
- ** 'down' day 3 v. 'down' days -1, 5, 6, and 7 (p<0.00004)
- ** 'down' day 4 v. 'down' days -1, 7 (p<0.00006), and 6 (p<0.04)
- ** 'down' day 5 v. 'down' day -1 (p<0.007)
- ** 'up' days 1 and 2 v. 'up' days -1, 3, 4, 5, 6, and 7 (p<0.00003)
- ** 'up' day 3 v. 'up' days -1, 6, and 7 (p<0.006)
- φ 'down' day 1 v. 'up' days -1, 1, 2, 3, 4, 5, 6, and 7 (p<0.02)
- φ 'down' days 2 and 3 v. 'up' days -1, 3, 4, 5, 6, and 7 (p<0.003)
- φ 'down' day 4 v. 'up' days -1, 4, 5, 6, and 7 (p<0.04)
- φ 'down' day 5 v. 'up' days -1, 6, and 7 (p<0.02)
- φ 'down' day 6 v. 'up' day 1 (p<0.02)
- φ 'down' day 7 v. 'up' days 1 and 2 (p<0.007)
- # interaction of group x time (p<0.004)

time (minutes), intensity (% HR_{max}), and speed (% 10 km time), it is recognised that expression of race speed as a percentage of the 10 km personal best time may mask differences in the rate of stretch-shortening cycle exercise during the ultramarathon race. Although it may be argued that differences in absolute running speed are associated with differences in loading forces, the differences in this study were subtle and arguably not a major factor associated with the development of the muscle damage.

Plasma creatine kinase (CK) activity is a commonly used indicator of muscle damage.²² Plasma CK activity was significantly higher after the 'down' run, compared with the 'up' run, and remained significantly elevated for 5 days compared with pre-race values in the 'down' group, whereas in the 'up' group, values had returned to pre-race values by day 4 after the Comrades marathon. These findings are consistent with other studies that also reflect a rapid increase in CK activity from 24 hours after a marathon.^{22,27} Kryöläinen *et al.*²² reported peak plasma CK activity of 1147±520 U.l⁻¹ 2 days after a marathon. Conversely, after high-force eccentric exercise protocols, for example, maximal contraction of the elbow flexors, the

increase in CK activity does not begin until approximately 48 hours after the exercise, with peak CK activity occurring only between 4 - 6 days following the exercise.⁷ The differences in plasma CK activity following downhill running and high-force eccentric exercise protocols is well-documented;⁷ however, the underlying mechanism for the different responses is unclear.

This is the first study to demonstrate a difference in the CK response to ultra-endurance exercise. It may be hypothesised that the difference in CK activity between the 'down' and 'up' groups is related to the increased amount of downhill running during the 'down' Comrades marathon compared to the 'up' Comrades marathon, and therefore the greater magnitude of eccentric (muscle-lengthening) action during the 'down' run. Studies have shown a dissociation between CK activity and the extent of exercise-induced muscle damage,^{26,30} therefore one should interpret the magnitude of CK activity as a direct marker of muscle damage with caution. However in this study, as pain was also elevated it is logical to conclude that the 'down' group did indeed have more muscle damage.⁷

There was also a large degree of intra-subject variability in plasma CK activity, particularly in the 'down' group at days 1 and 2 after the Comrades marathon. This individual variation in CK activity may be associated with differences in the rate of CK clearance by muscle and the reticuloendothelial system,⁸ and not related to physical activity, gender, or muscle mass.⁷ Unfortunately the design of this study cannot provide an explanation for the large degree of intra-individual variation in CK activity. Further studies are needed to investigate this finding.

In conclusion, the 'down' Comrades marathon causes more muscle pain and plasma CK activity compared with the 'up' Comrades marathon. Subjective pain scores remained elevated for at least 7 days after the 'down' race, but only for 4 days after the 'up' race. Further studies are required to accurately define the regeneration of muscle following the Comrades marathon after the symptoms of damage have disappeared.

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