Increased running speed and pre-race muscle damage as risk factors for exercise-associated muscle cramps in a 56 km ultra-marathon: A prospective cohort study

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Increased running speed and pre-race muscle damage as risk factors for exercise-associated muscle cramps in a 56 km ultra-marathon: a prospective cohort study

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ABSTRACT

Background Despite the high prevalence of exercise-associated muscle cramping (EAMC) in endurance runners, the aetiology and risk factors for this condition are not fully understood.

Purpose The purpose of this prospective cohort study was to identify risk factors associated with the development of EAMC in ultra-distance runners.

Methods 49 runners participating in a 56 km race completed a validated pre-race questionnaire. Pre-race muscle pain in the calves, hamstrings and quadriceps muscles was recorded (visual analogue scale) and pre-race serum creatine kinase (CK) activity was measured. 20 runners reported EAMC (EAMC group) during or within 6 h after the event, while 29 runners reported no cramping (CON group).

Results EAMC was not associated with age, body mass index, sex, recent and past personal best running times, pre-race muscle pain and pre-race training (duration and frequency). Runners in the EAMC group tended to report on average longer training sessions during the 3 days before the race (EAMC 1.2 (1.1), CON 0.6 (1.0); $p=0.077$). Significant risk factors for EAMC were a past history of EAMC (EAMC 100%, CON 48%; $p<0.001$) and a faster running time (min) for the first 28 km split time of the race (EAMC 144 (20), CON 157 (14); $p=0.029$) despite being matched for recent (<15 weeks before race) personal best times in the 42.2 km race. Pre-race CK activity tended to be higher in the EAMC group (EAMC 89 (80), CON 58 (35); $p=0.066$).

Conclusions Novel risk factors for EAMC in distance runners are a past history of EAMC, faster running pace at the early stage of a race and possibly pre-race muscle damage.

During a race, exercise-associated muscle cramping (EAMC) is one of the most common medical problems encountered by ultra-distance runners.[1] EAMC can be defined as a syndrome of involuntary painful skeletal muscle spasms that occur during or immediately after physical exercise,[2 3] and clinically presents as painful localised muscle cramping that occurs spasmodically in different exercising muscle groups—usually the calf, hamstring or quadriceps muscles.[3 4]

Despite the fact that EAMC is common in ultra-distance runners, the aetiology of and risk factors for the condition are still not well understood,[4–6] and have recently been reviewed.[4] Heat,[7] dehydration[7] and electrolyte depletion[5 6 8] are the more traditional hypotheses for the cause of EAMC,[2] despite the fact that evidence supporting these traditional hypotheses is limited.[4] Data from a number of prospective cohort studies show no relationship between serum electrolyte changes and the development of EAMC,[9–12] or measures of dehydration and the development of EAMC.[9 11 12] However, it appears that athletes, coaches and scientists still remain to be convinced that dehydration and electrolyte depletion are not necessarily related to the development of EAMC.[5 6 13–17]

More recently, there has been increasing evidence that a number of factors may result in the development of abnormal neuromuscular control during exercise, and these factors may all predispose to the development of EAMC.[4] First, it has been documented that the development of muscle fatigue during exercise increases muscle spindle afferent activity and decreases Golgi tendon organ afferent activity,[18 19] which may result in increased α motor neuron activity. Therefore, as progressive muscle fatigue develops, there may be an increased risk of developing EAMC.[2] Second, it has been shown that there is increased baseline electromyographic activity in triathletes with EAMC immediately after the race, when compared with a non-exercising control muscle.[12] Third, and most recently, it has been shown in a large prospective cohort study in more than 200 triathletes that competing at a pace that is faster than their usual training pace (higher relative exercise intensity) is an independent risk factor for the development of EAMC.[9] This novel risk factor has not been reported in another population of athletes that are at risk of the development of EAMC such as ultra-distance runners.

Finally, in a recently published review, it has been suggested that muscle injury or muscle damage could result in 'reflex muscle spasm', and that this could be a potential mechanism for the development of EAMC.[4] For example, high intensity or prolonged training in the days leading up to an ultra-endurance running event could potentially increase the risk of subclinical muscle damage. Therefore, failure to taper for a race could be a predisposing factor for the development of EAMC. However, this hypothesis has to our knowledge not been investigated to date.

The aim of this prospective cohort study was therefore to identify risk factors that are associated with the development of EAMC in runners who participate in a 56 km race. More specifically, we wanted to investigate whether running at a pace that is faster than the usual running pace is an independent risk factor for the development of EAMC in ultra-marathon runners, and whether pre-race muscle damage could be a a risk factor for the development of EAMC.

METHODS

Subjects

All 5824 ultra-marathon runners who completed the 2009 Two Oceans ultra-marathon within the 7 h cut-off time were regarded as potential subjects for this prospective cohort study. The study protocol was approved by the Human Research Ethics Committee of the University of Cape Town (REC 066/2009). Runners were informed about the study during the 3-day registration period before the race. A research area was established at the race registration venue, where potential subjects were approached and informed of the nature of the study. All interested runners were then required to give their written informed consent for the study. Once written informed consent was obtained, runners completed a detailed, previously validated pre-race questionnairre.[9 11 12 20] In most instances, the runners completed the questionnaire during registration. In a small percentage of cases, runners were given the questionnaire to complete at their own leisure and to return it by post or email. Of a total of 151 runners who completed the pre-race questionnaire, 49 runners agreed to participate in the prospective cohort component of the study.

Pre-race serum CK activity determination

All recruited runners were also asked to donate a 5 ml blood sample for determining pre-race serum creatine kinase (CK) activity as an indirect measure of pre-race muscle damage. Blood samples were collected into tubes containing lithium heparin, and were kept on ice until centrifugation at 2000g for 10 min at 4°C. Samples were stored at −20°C until the analysis of serum CK activity. Plasma CK activity was measured by spectrophotometric (Beckman DU-62; Beckman Instruments, Fullerton, California, USA) enzymatic assays (CK-NAC activated, Automated Analysis for BM/Hitachi Systems 704; Boehringer Mannheim, Meylan, France).

Pre and post-race muscle pain scoring

In the 3 days before the race runners were also asked to document their muscle pain graphically on a visual analogue scale (100 mm) to indicate the severity of muscle pain. This scale involved documenting self-reported muscle pain under four conditions: at rest; during daily activity; during passive stretching and when applying pressure to the muscle. Pain was documented in a selected group of muscles including the following: calves; hamstrings and quadriceps muscles. Runners were requested to report to the medical facility at the race finish to document their post-race muscle pain scores using the same visual analogue scale.

Documentation and diagnosis of EAMC

Ay the time of recruitment, all runners were informed about the symptoms and signs of EAMC, and were requested to report to a designated area in the medical facility at the race finish. Runners who experienced EAMC during or immediately after the race were assessed by a sports physician to verify the diagnosis using established clinical criteria.[21] A total of 20 runners developed EAMC (EAMC group) during or immediately after the 56 km ultra-marathon race and a group of 29 runners did not develop cramping (CON group) during or immediately after the race. These runners constituted the final cramp group (EAMC 20 and those runners who did not experience EAMC acted as the control group (CON 29).

Statistical analysis of data

All the pre and post-race data were entered onto an Excel spreadsheet. Statistical analyses were performed on these data using the Statistica 9.0 program.With the exception of muscle pain scores, which were expressed as scatter plots and median, all the numerical data are represented by the mean±SD, with the number of runners (N) with non-missing data being represented in parenthesis. A one-way analysis of variance was used to determine any significant differences of normally distributed continuous data and categorical data were analysed using the χ^2 test. A Mann–Whitney test was used to analyse non-parametric data. Statistical significance was accepted with $p<0.05$.

RESULTS

General characteristics of participants

The personal characteristics of the 20 participants of the 2009 Two Oceans marathon who reported EAMC (EAMC group) and the group of 29 runners who reported no cramping (CON group) during or immediately after the event are depicted in table 1. No statistically significant differences were found for age, height, weight, body mass index (BMI) or sex when the two groups were compared.

All runners (100%, N=20) who reported cramping during or immediately after the ultra-marathon had a self-reported past history of EAMC, while only 48.1% (N=13 of 27) of the CON group had a past history of EAMC ($p<0.001$). Only six runners (22.2%) within the CON group reported EAMC during the past year while 14 runners (70.0%) in the EAMC group reported EAMC during the last year ($p=0.001$).

Training history and race performance

The training frequencies, distances run and duration of training of the runners, during the 15-week period before the race, as well as their personal best and recent running times for running distances 10, 21.1 and 42.2 km, and events such as the 56 km Two Oceans and 89 km Comrades ultra-marathons for the EAMC and CON groups are summarised in tables 2 and 3. There were no significant differences between the career and recent personal best times between the two groups for any

Table 1 Personal characteristics of the runners who reported EAMC during or immediately after the 2009 Two Ocean marathon compared with control runners

	EAMC group (N=20)	CON group (N=29)	p Value
Age (years)	40.8±11.7 (19)	40.2±9.2 (29)	0.857
Height (cm)	176.4±6.8 (13)	173.9±9.6 (26)	0.406
Weight (kg)	73.7±10.9 (18)	71.9±11.0 (29)	0.587
BMI (kg/m²)	23.6±2.8 (13)	24.1±3.0 (26)	0.643
Sex (% males)	95.0 (20)	79.3 (29)	0.216

Except for sex, which is expressed as a frequency, all other values are expressed as an average±SD. The number of runners (N) with non-missing data for each variable is in parentheses. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared.
CON, control; EAMC, exercise-associated muscle cramping.

particular running distance or specific event (table 2). During the 15 weeks before the race, it was noted that, although not statistically significant, the training time within the 3 days before the event was higher (p=0.077) for the EAMC group when compared with the CON group (table 3). However, no significant differences were noted for the training times for the last 2 days before the event. Similarly, there were no significant differences encountered in the total training frequency, duration of training, intensity of training, or employment hours between the two groups leading up to the event.

Running performance

The actual performance times, pre-race performance times as well as the relative performance times of the runners for the Two Oceans marathon were documented. There were no significant differences in the pre-race predicted 42 km split times or the overall 56 km finishing times between the EAMC or CON groups (data not shown).

However, the runners in the EAMC group completed the first half of the race (28 km split time) in a significantly faster time (144.3±20.2 min) than those in the CON group (157.0±14.3 min; p=0.029). There were no significant differences between groups in the following times: the time for the second 28 km of the race, the time for the last 14 km of the race, the 42 km split time and the overall finishing time (data not shown).

Table 2 The career and recent personal best times for various road events of the runners who reported EAMC during or immediately after the 2009 Two Ocean marathon and control runners

	EAMC group (N=20)	CON group (N=29)	p Value
Career personal best times			
10 km (min)	39.4±5.2 (8)	42.29±6.5 (21)	0.148
21.1 km (min)	119.9±81.5 (17)	97.7±15.9 (26)	0.518 [a]
42.2 km (min)	213.3±42.0 (18)	217.6±23.7 (26)	0.403 [a]
56 km Two Oceans (min)	310.1±41.3 (15)	322.2±37.4 (19)	0.376
89 km Comrades (min)	556.9±151.2 (14)	576.4±72.6 (18)	0.633
Recent (past 15 weeks) personal best times			
10 km (min)	45.5±11.8 (8)	48.9±8.1 (12)	0.449
21.1 km (min)	124.8±88.8 (14)	114.3±18.3 (16)	0.646
42.2 km (min)	253.6±65.9 (16)	242.8±29.4 (26)	0.403

Personal best times are expressed as an average±SD. The number of runners (N) with non-missing data for each variable is in parentheses.
*Non-parametric p value.
CON, control; EAMC, exercise-associated muscle cramping.

Table 3 The training history (frequency, distances and durations) of the runners who reported EAMC during or immediately after the 2009 Two Ocean marathon and control runners during the 15-week period before the 2009 Two Oceans ultra-marathon

	EAMC group (N=20)	CON group (N=29)	p Value
Training frequency (days/week)	4.36±1.3 (18)	4.15±1.4 (26)	0.616
Training distance (15 weeks) (km/week)	55.3±18.8 (19)	51.8±23.2 (26)	0.589
Training duration (15 weeks) (h/week)	6.5±2.9 (18)	5.6±2.1 (26)	0.516 [a]
Training distance (1 week) (km)	26.5±28.8 (19)	31.8±30.2 (27)	0.560
Training duration (1 week) (h)	2.9±2.1 (18)	3.5±3.2 (24)	0.537
Hard training sessions (8 weeks) (per week)	4.3±7.2 (20)	4.3±4.2 (26)	0.999
Training intensity at race speed (%)	48.8±33.5 (17)	62.9±24.4 (26)	0.118
Training duration (3 days) (h)	1.1±1.1 (17)	0.6±1.0 (26)	0.077
Training duration (2 days) (h)	0.5±0.3 (16)	0.3±0.6 (26)	0.291

Data are expressed as an average±SD. The number of runners (N) with non-missing data for each variable is in parentheses.
*Non-parametric p value.
CON, control; EAMC, exercise-associated muscle cramping.

Past medical history of the runners

Past general medical conditions in the runners were considered as possible risk factors for EAMC during or immediately after the Two Oceans ultra-marathon (table 4).

Only a past history of exercise-associated collapse was shown to be significantly different between the EAMC (15.0%) and the CON (0%) group (p=0.041). There was no significant difference in the family history of EAMC (p=0.507) or nocturnal cramping (p=0.802) between the two groups (data not shown).

Flexibility training

There was a significant difference (p=0.026) between the number of runners stretching before exercise who experienced EAMC compared with the CON group, with 92.9% (n=14) of the EAMC group stretching before exercise versus 54.6% (n=11) of the CON group. Although not significant (p=0.131), it was noted that 70.0% (14 of 20) of the EAMC group followed a flexibility training programme compared with only 48.3% (14 of 29) of the CON group. There was also a tendency (p=0.070) for the EAMC group to stretch for longer at 9.8±23.8 min/week compared with the CON group who stretched for 1.1±2.5 min/week. No significant differences were observed between the two groups for stretching during exercise (p=0.599) or after exercise (p=0.280).

Pre-race serum CK activity

The serum CK activity of the runners was determined from samples taken before the event to document if there was any evidence of pre-race muscle damage. The pre-race serum CK activity tended (p=0.066) to be higher in the EAMC group (89.1±80.1 units, N=20) when compared with the CON group (58.1±34.9 units, N=30).

Pre-race perceived muscle pain

The perceived pain (at rest, during daily activities, during passive stretching and when applying pressure) to the muscle was compared between groups. There were no significant

Table 4 General medical conditions that were self reported in the pre-race runners with EAMC during or immediately after the 2009 Two Ocean marathon and the control group

	EAMC group (N=20)	CON group (N=29)	p Value
Tendon ligament injury (% yes)	45.0 (20)	44.8 (29)	0.990
Flu symptoms (% yes)	42.1 (19)	29.6 (27)	0.382
Medication (% yes)	57.9 (19)	55.2 (29)	0.853
GIT symptoms (% yes)	50 (20)	61.5 (26)	0.431
Nervous system (% yes)	5 (20)	11.1 (27)	0.759
Allergies (% yes)	15.8 (19)	28.6 (28)	0.310
Asthma (% yes)	5.0 (20)	3.9 (26)	0.849
Current injury (% yes)	65.0 (20)	64.3 (28)	0.959
Collapse (% yes)	15.0 (20)	0.0 (26)	0.041

The values are expressed as frequencies (%),with the number of runners (N) in parentheses.
CON, control; EAMC, exercise-associated muscle cramping; GIT, gastrointestinal tract.

differences in pre-race perceived pain in the hamstrings and calf muscle components between the EAMC group and the CON group. However, the EAMC group perceived significantly more post-race pain in their quadriceps muscle groups (during stretching of the muscle and when applying pressure to the muscle) compared with the CON group (p=0.009 for stretching and p=0.02 when pressure was applied, respectively).

DISCUSSION

The main findings from this prospective cohort study were that the independent risk factors for EAMC were a past history of EAMC, faster running time for first 28 km split time of the ultra-marathon, previous history of collapse, more stretching before exercise, increased exercise duration (last quarter of the event) and greater quadriceps muscle pain scores post-race.

The first main finding of this study was that runners in the EAMC group had a faster first 28 km split time of the marathon compared with the CON runners (p=0.014), which indicates that runners in the EAMC group competed at a faster pace early on in the race. This is indirect evidence that runners in the EAMC group exercised at a higher relative intensity compared with the runners in the CON group during the first 28 km of the event. This finding is similar to the finding that has recently been reported in a large prospective cohort study in Ironman triathletes.[9] In the studyin Ironman triathletes,[9] it was shown that the development of EAMC was associated with faster predicted race times and faster actual race times, despite similarly matched preparation and performance histories in subjects from both groups.

It is important to note that in our study, the analysis of the personal best career of the two groups also yielded no significant differences for the various running distance events. This indicates that both groups were also similarly matched for running ability. Furthermore, in our study, the runners in the EAMC and CON groups reported similar training frequencies before the race. However, in the 15-week period leading up to the event, there appeared to be a tendency for longer training sessions in the EAMC group. The time spent training within the 3 days preceding the event also tended to be higher in the EAMC group.

Therefore, results from two prospective cohort studies now show that even though an EAMC group and a control group have similar athletic ability, the athletes (runners or tri-athletes) in the EAMC group competed at a faster pace. These athletes would thus have an increased risk of developing early muscle fatigue, which could have made them more susceptible to EAMC.

In our study it is of particular interest when this finding is interpreted together with the novel observation showing a tendency of the pre-race serum CK activity to be higher in the EAMC runners compared with the CON runners (p=0.066). This tendency may indicate a greater degree of subclinical pre-race muscle damage in the runners in the EAMC group. This finding is also in keeping with the observation that pre-race training volume in the EAMC group tended to be greater in the 3 days before the race. The combination of subclinical pre-race muscle damage together with increased exercise intensity in the early parts of the ultra-marathon race may well be a predisposing factor for the development of EAMC in this group. However, the small sample size is a limitation of the present study, and it is clear that more studies are needed to explore these relationships, using larger sample sizes.

The perceived pre-race muscle pain in the quadriceps muscle group, during stretching of the muscle and when applying pressure to the muscle groups, was not different between groups. However, these muscles were significantly more painful in the EAMC group after the race. The quadriceps muscle group is commonly involved in EAMC, is the primary extensor of the legs during running, and is more vulnerable to eccentric damage during running. EAMC occurs in the most active muscle groups, and in runners these are the hamstring muscles, the calf muscle groups and also the quadriceps groups.[1 21] It is also known that the muscle groups most prone to cramping are those that span across two joints.[13 22] It is important to note that the increased post-race perceived pain in the muscles of the EAMC group may either be a cause of the EAMC or may be as a consequence of the development of EAMC. This could not be determined from this study design and requires further investigation.

In most of the runners, cramping occurred in the fourth quarter of the endurance event. This supports previous observations that increased exercise duration is a risk factor for EAMC.[10 22]

All the runners (100%, N=20) who reported cramping during or immediately after the ultra-marathon had a self-reported past history of EAMC, while only 48.1% (N=13 of 27) of the CON group had a past history of EAMC (p<0.001). This finding is similar to that reported in a recent prospective cohort study in tri-athletes.[9]

A further finding of our study was the association between a self-reported past history of collapse in runners with EAMC. There is no clear reason for this observation, but it may indicate that there is a muscular or neuromuscular abnormality in runnerswith a past history of collapse that only manifests during prolonged running. This association may therefore be related to an underlying subclinical systemic disorder in the runners, and it is suggested that this association be investigated further.

Another finding in our study was that a higher percentage of the runners in the EAMC group performed stretching and flexibility training before exercise. This may be either a cause or a consequence of EAMC, and the relationship between flexibility training and EAMC therefore requires further investigation.

Finally, in this prospective cohort study, no association between EAMC and the following risk factors were found: increased age, increased height, higher BMI, positive family history of cramping or a positive past history of tendon/ligament injury. These observations are in keeping with those reported in a prospective cohort study in tri-athletes.[9]

As menitoned, the main limitation of our study design was a relatively small sample size that limited an analysis of risk factors in subgroups of runners with EAMC. However, the main strength of our study is that the design was a prospective cohort study, which is the design of choice to determine risk factors for illness and injury. Furthermore, the present study remains one of only two prospective studies on EAMC in distance runners.

CONCLUSIONS

The main findings from this prospective cohort study were that the independent risk factors for EAMC were a past history of EAMC, a faster running time for the first 28 km split time of the ultra-marathon, previous history of collapse, more stretching before exercise and increased exercise duration (last

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What is already known on this topic

One of the most common medical conditions in distance runners is EAMC. Despite this, there is still controversy surrounding the aetiology and risk factors for this condition. The most common hypotheses for the cause of EAMC are electrolyte depletion and dehydration. However, recent evidence indicates that exercise at a higher intensity (faster pace) may be responsible for EAMC.

What this study adds

The results of this study show that independent risk factors for EAMC in runners were a past history of muscle cramping (in particular the number of EAMC reported in the last 10 races) and an overall faster running pace in the first 28 km of a 56 km race. Furthermore, failure to taper just before the race may be associated with subclinical muscle damage and this can also predispose to the development of EAMC during the race.

quarter of the event). In addition, there was a tendency that pre-race muscle damage and training in the few days before the race were greater in the cramping runners.

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Competing interests None.

Ethics approval This study was conducted with the approval of the Research Ethics Committee of the Faculty of Health Sciences, University of Cape Town.

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