Muscle Damage and Fatigue in the Marathon

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27:4; 45-55, 2012

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ABSTRACT

Is muscle fatigue in the marathon related to body mass change (dehydration) and/or muscle damage produced by the continuous foot strikes over the 42.2km distance? For this study, adapted from a paper originally published in Applied Physiology Nutrition and Metabolism Journal, amateur runners (114 men and 24 women) were tested before a marathon for leg muscle power output, their body weight was recorded and a urine sample was obtained. Within three minutes of completing the race, run in 28°C and 46% relative humidity, the subjects repeated the leg power test and then their body weight and urine samples were collected again. The authors found that mean body mass reduction was 2.2±1.2%. The body mass change shows high inter-individual variability, but only 7% of the runners studied lost more than 4%. No myoglobin (a protein indicating muscle fibre damage) was detected in the pre-race urine specimens while post-race urinary myoglobin concentration increased to 3.5±9.5 µg·mL-1 (P<0.05). Mean leg muscle power reduction after the race was 16±10%. Muscle power change significantly correlated with post-race urine myoglobin concentration (r=-0.55; P<0.001) but not with body mass change (r=-0.08; P=0.35). The correlation between myoglobinuria and muscle power change suggest that muscle fatigue is associated with muscle tissue breakdown.

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Introduction

The ingestion of water and/or sports drinks during prolonged running has been found to be an effective method to maintain cardiac output, regulate temperature (MONTAIN & COYLE, 1992) and preserve muscle performance (COSO et al., 2008). However, the recommendable amount of liquids while running is still under debate (CHEUVRONT et al. 2007). International experts have provided guidance on appropriate fluid replacement during exercise based on experimental evidence (SAWKA et al., 2007; RODRIGUEZ et al., 2009). Assuming proper pre-exercise hydration status, drinking during running should prevent body mass loss above 2%, avoid excessive body water deficit and reduce the risk of exertional heat illnesses (CASA,1999).

A different point of view has been proposed by NOAKES (2007a, 2007b); who indicates that during evolution, human beings developed biological adaptations (multiplication of eccrine sweat glands, reduced body hair, a thirst mechanism based on serum osmolality, etc.) to enhance the capacity of running long distances in the heat. According to this author, runners should drink only when they are thirsty because this strategy would be effective in avoiding excessive dehydration but also to prevent overdrinking and hyponatremia. It is common that individuals dehydrate by more than 2% when using the thirst stimulus to replace fluid during exercise (PASSE et al., 2007). Although the deleterious effects of dehydration >2% on endurance performance has been well established in laboratory studies (SAWKA et al., 2007) elite marathon runners dehydrated by more than 2% during real competitions, including even the winners of the most important races (BEIS et al., 2012).

The muscle breakdown derived from prolonged running could be a key factor affecting performance during endurance running events (RAMA et al., 1994). MEYER-BETZ (1910) first described a post-exertion syndrome that included severe muscle pain, weakness and brown urine. Currently, this syndrome is known as exertional rhabdomyolysis and is defined as muscle fibre damage derived from strenuous exercise, producing the release of muscle proteins (mainly myoglobin) into the blood stream. Exertional rhabdomyolysis is accompanied by severe damage in the muscle fibres, the sarcolemma, T-tubules and myofibrils, thus negatively affecting the capacity of the muscle to generate force (CLARKSON & SAYERS, 1999). Several studies have reported a decline in the ability to generate force after muscle fibre damage, mainly in eccentric muscle actions (BROWN et al., 1996; KIRBY et al., 2011). Running involves both concentric and eccentric muscle actions of lower intensity than the ones found in experimental investigations (FRIDEN et al., 1983; BROWN et al., 1996; CLARKSON et al., 2006). It has been reported that elite marathon runners lose 22% of their maximal force production in the knee extensors and power during a countermovement jump decreases by 13% (PETERSEN et al., 2007). However, there is no information to assess whether the reduction in muscle force and power following a marathon is related to muscle damage or dehydration, especially in heat conditions.

The purpose of this study was to determine the body mass change and urinary myoglobin concentration in recreational runners after a marathon run in a warm environment. A second objective was to determine whether runners with high levels of body mass loss and/or myoglobinuria presented greater losses of muscle power following the marathon.

METHODS

Participants

The data presented in this study correspond to 138 marathon finishers. Their main morphological characteristics and training status before the race are summarised in Table 1. All of the participants had previously com-

Table 1: Morphological characteristics, training status and race time of the study participants (Data are mean ± SD for 138 healthy marathon runners completing the Madrid Marathon.)

n	Age (yr)	Weight (kg)	Height (cm)	Body fat (%)	Training status*	Race time (min)
138	39 ± 8	72 ± 11	173 ± 8	13 ± 5	2.2 ± 0.7	229 ± 38

Training status: 1 = from 0 to 35km a week; 2 = from 36 to 70km a week; 3 = from 70 to 105km a week; 4 = more than 105km a week, according to Smith et al. (2004).

pleted a marathon race. Participants were fully informed of any risks and discomforts associated with the experiments before giving their informed written consent to participate in the investigation. Before participation, volunteers completed a short questionnaire on training status and medical history. Potential participants with a history of muscle disorder, cardiac or kidney disease or those taking medication were excluded.

Experimental procedures

One to three days before the race, the participants underwent a physical examination to ensure that they were in good health. Their body fat composition was calculated using bioimpedance (BC-418, Tanita, Japan; (MOON et al., 2009)). Following this, they performed a five-minute warm-up consisting of dynamic exercises and submaximal jumps and they were thoroughly familiarised with the jump test. Each subject then performed two countermovement vertical jumps for maximal height on a force platform (Quattrojump, Kistler, Switzerland). For this measurement, participants began stationary in an upright position with their weight evenly distributed over both feet. The subjects placed their hands around their waists in order to remove the influence of the arms on the jump. On command, they flexed their knees ~90° and jumped as high as possible while maintaining their arms on their waist and then landed with both feet. After 1 min. of rest, the countermovement jump was repeated.

After the vertical jumps, a sterile container was provided to the runners and verbal instructions were given to collect a specimen from the first morning void the day of the race. Thirty minutes before the start of the race, participants arrived at the start line after their habitual warm-up. Participants brought the urine specimen and wore the same clothing to be worn during the marathon. Pre-race body mass was measured with a ± 50g scale (Radwag, Poland). Then, the participants went to the start line to complete the race with no instructions about pace or drinking.

The 42,195m of the race were completed with a mean dry temperature of 28 ± 1ºC and 46 ± 3 % relative humidity (range from 21 to 30ºC, temperature readings at 30-minute intervals from 0 to 5 hours after the race start). Within 3 minutes of completing the race, participants went to a finish area and performed two countermovement vertical jumps as previously described. Post-race body mass was recorded with the same scale and same clothes used for the pre-race measurement. Although post-race body mass measurement included the sweat trapped in the clothing this represents an error lower than 10% for the calculation of true hydration status (CHEUVRONT et al., 2002). Participants were instructed to avoid drinking until they were weighed and an experimenter was at the finish line to assure compliance. After that, subjects were provided with fluid (water and sports drinks) to hydrate and promote urine production. Thirty to 60 min-

utes after the race, a representative sample of the post-race void was collected in a sterile container and participants left the post-race setting area. Participants were contacted via email in the following days to report any major medical problem.

The urine sample obtained in the morning of the marathon and the urine sample obtained 60 minutes after the race were immediately analysed (within 2 hours) for specific gravity (Usg), pH, protein, glucose, ketones and bilirubin concentrations and the presence of leukocytes and erythrocytes by using reactive strips (Combur Test, Roche, Switzerland), as previously described (ABIAN-VICEN et al., 2012). For these measurements, the strip was dipped in the urine sample and the excess was wiped off with a clean and absorbent paper. Then, the test strip was placed on the tray of a photometer (Urisys 1100, Roche Switzerland) and the aforementioned variables were measured after 1 minute of incubation. A representative portion (5 mL) of the urine sample was frozen at –80ºC. Urine myoglobin concentration was determined by using immunoluminiscence at a later date.

Statistical analysis

Initially, we tested the normality of each variable with the Kolmogorov-Smirnov test. Changes in the variables from pre- to post-race were analysed with Student's t-test for paired samples. To simplify the presentation of body mass change data, the subjects were grouped by using 1% intervals. Similarly, they were grouped by their change in leg muscle power by using 10% intervals. Urine variables were also presented by the frequency of subjects that presented a determined value. We used Pearson's correlation to assess the association between two variables. The significance level was set at $P < 0.05$. The results are presented in Table 2 as mean ± SD.

RESULTS

Body mass change

During the race, most subjects reduced their pre-race body mass (from 71.9 ± 10.8 to 70.3 ± 10.7 kg; $P < 0.05$) but the individual responses were very heterogeneous (Figure 1). Mean body mass loss after the race was 2.2 ± 1.2%,

Table 2: Urine responses before and after a marathon race (Data are mean ± SD for 138 healthy runners completing a marathon in the heat. The table includes the frequency for several categories in the urine specific gravity (U_{sg}), haematuria, leukocyturia, proteinuria, ketonuria and bilirubinuria).

	Pre	Post	P value
U_{sg}	1.017 ± 0.005	1.017 ± 0.005	0.6
pH	5.9 ± 0.9	5.8 ± 1.1	0.2
Haematites	0.4 ± 0.6	23.2 ± 61.0	< 0.05
Leukocytes	0.0 ± 0.0	7.8 ± 46	< 0.05
Proteins	6.1 ± 6.0	42.6 ± 80.1	< 0.05
Ketones	0.0 ± 0.0	3.0 ± 6.4	< 0.05
Bilirubin	0.1 ± 0.3	0.4 ± 0.6	< 0.05

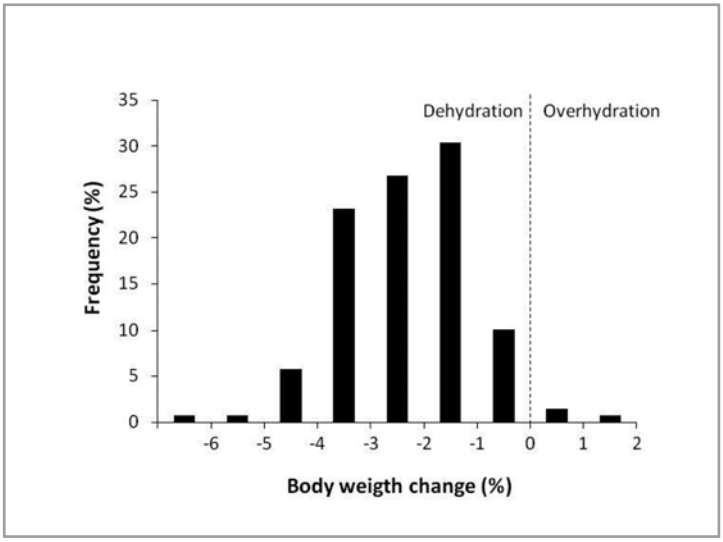

Figure 1: Body mass change after a marathon in a warm environment (Data are frequencies for 138 amateur marathon runners.)

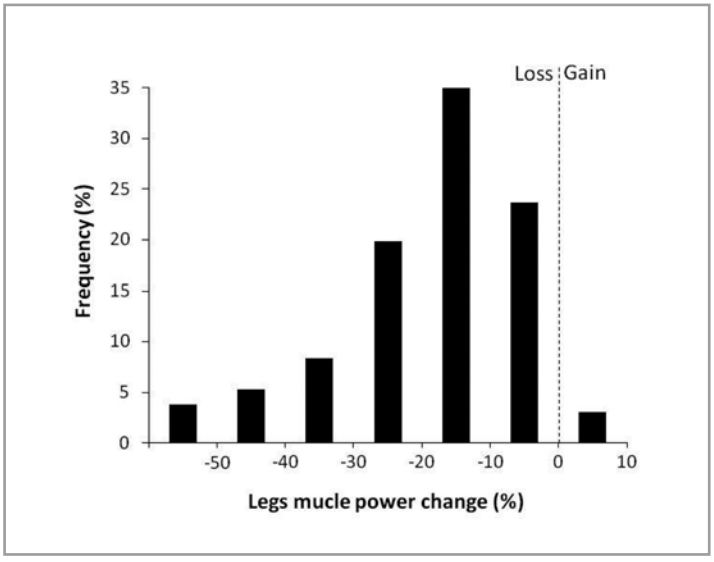

Figure 2: Pre-to-post marathon changes in leg muscle power during a countermovement jump (Data are frequencies for 138 amateur marathon runners.)

with 55 runners (40% of the total) reducing their body mass by less than 2%. Only 10 subjects (7.2% of the sample) reduced their body mass by more than 4% with one of them peaking at 6.2% of body mass loss. On the contrary, three runners increased their pre-race body mass with a maximal gain of 1.3% (overhydration).

Race time and leg muscle power change

Mean race time was 229 ± 38 minutes (range from 151 to 301 min) with 96 subjects finishing the race under 240 minutes. Before the race, mean power output during the concentric phase of the jump was 22.5 ± 4.9 W·kg^{-1} and jump height was 24.0 ± 5.8 cm. After the race, jump power output (18.9 ± 5.6 W·kg^{-1}; $P < 0.05$) and jump height (19.2 ± 6.3 cm; $P < 0.05$) were significantly reduced by 16 ± 10% and 20 ± 10%, respectively. However, similarly to body mass change, the individual responses were very heterogeneous (Figure 2). A total of 109 subjects (79% of the sample) reduced their muscle power by less than 30%. Still, 24 subjects reduced their leg muscle power by over 30% (maximal reduction was 62%) while four subjects slightly increased leg muscle power (maximal increase was 6%).

Urine analysis

The morning before the race, 122 subjects had first-morning U_{sg} below 1.020. Only 16 (12% of the sample) exceeded 1.020 with no individuals above 1.025. U_{sg} did not change from pre to post race (Table 2). However, the race produced a significantly higher presence of erythrocytes and leukocytes in the urine and increased the mean concentration of proteins, ketones and bilirubin (Table 2; $P < 0.05$). No myoglobin was detected in the pre-race urine specimens, but post-race urinary myoglobin concentration increased to 3.5 ± 9.5 µg·mL^{-1}. A total of 120 subjects presented urinary myoglobin concentrations lower than 1µg·mL^{-1} after the race. Only 12 (9%) had urinary myoglobin levels higher than 10 µg·mL^{-1} while peak concentration was 52.3 µg·mL^{-1}.

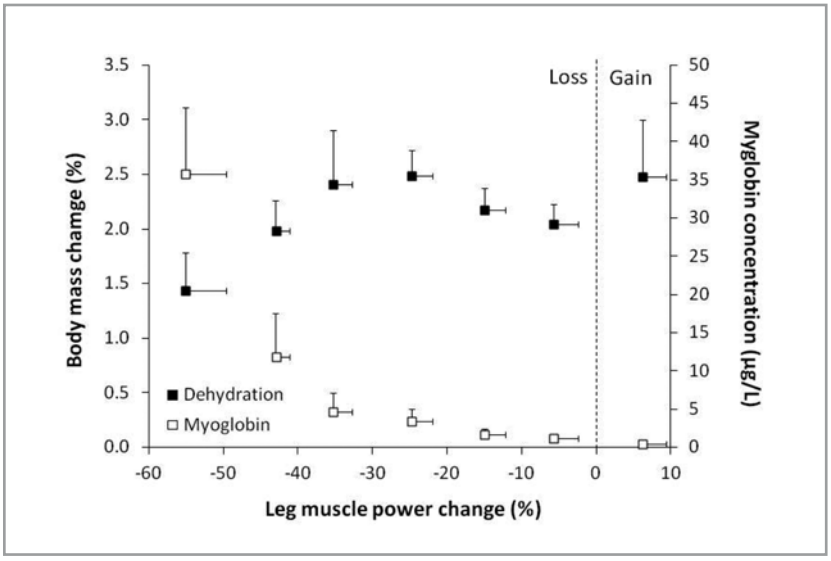

Figure 3: Body mass loss (A) and urinary myoglobin concentration after a marathon in a warm environment (B) according to the changes in leg muscle power (Data are mean ± SD for 138 amateur runners grouped by their muscle power loss after the marathon.)

Correlations

Figure 3 depicts the mean body mass change experienced by the runners according to their change in leg muscle power production. There was no significant correlation between the body mass change during the race and the change in leg muscle power production ($r = -0.08$; $P = 0.35$). On the contrary, we found a significant correlation between the change in leg muscle power production and the myoglobin concentration found in the post-exercise urine samples ($r = -0.55$; $P = 0.01$). In this case, those runners with high losses in muscle power output were also the participants with higher myoglobin content in urine. The hydration status and urinary myoglobin concentration were not correlated ($r = -0.06$; $P = 0.48$). Finally, race time was not correlated with the change in leg muscle power production ($r = 0.01$; $P = 0.90$) or post-race myoglobinuria ($r = 0.06$; $P = 0.48$).

DISCUSSION

The aim of this study was to investigate the body mass change and the muscle damage attained by recreational runners following a marathon race in a warm environment. A second objective was to determine whether runners with high levels of body mass loss and/or muscle damage presented greater losses of muscle power following the marathon competition. For these purposes, we recruited a heterogeneous group of 138 recreational runners, all with previous experience in the marathon, and measured pre- and post-race body mass and muscle power, and obtained urine samples.

The main findings of this study were that in amateur runners (a) mean body mass loss after the marathon race was 2.2 ± 1.2% with 10 participants (7.2% of the sample) reduced their mass by more than 4%. Only three runners slightly increased their pre-race body mass (Figure 1); (b) the marathon reduced the capacity to generate power during a countermovement jump by 16 ± 10%. Interestingly, those runners with higher levels of muscle power loss were the ones with higher levels of urinary myoglobin, a marker of muscle breakdown (Figure 3); (c) the marathon in a warm environment caused several urinary abnormalities (Table 2), most of them related to reduced flux to the kidneys.

Current guidelines for fluid ingestion during running indicate that the goal of drinking during exercise is to prevent excessive (> 2%) body mass loss (SAWKA et al., 2007). This recommendation is research based since current evidence indicates that adequate fluid ingestion during exercise enhances athletic performance, prevents a fall in plasma volume, cardiac output and skin blood flow, lowers rectal temperature and the perception of effort and prevents heat illnesses, especially in endurance events staged outdoors (SAWKA et al., 2007). These guidelines have substantially helped marathon runners to be well aware of the importance of drinking during exercise, particularly in hot environments.

However, marathoners do not always conform to the guidelines for fluid replacement. For example, PASSE et al. (2007) tested 18 runners with ***ad libitum*** access to sports drinks during a 10 mile (16km) run. Runners replaced 31% of the sweat loss and reduced their body mass by 1.9% during the run, suggesting that runners voluntarily dehydrated. BEIS et al. (2012) measured body mass changes in nine marathon winners and one second placer and found a mean body mass loss of 8.8%. In the present study, participants had free access to water and sports drinks during the race at 5km intervals, but we carefully refrained from advising them about fluid ingestion to avoid interfering with their normal practice. Interestingly, 40% of the subjects reduced their body mass by less than 2%, according to current fluid ingestion guidelines. Nevertheless, fifty percent of the subjects reduced their body mass between 2 and 4% while only 7.2% dehydrated excessively (body mass reduction higher than 4%). Hence, during this marathon race in a warm environment most runners have a slightly higher body fluid deficit than is scientifically recommended.

According to GANDEVIA (2001), muscle fatigue is an exercise-induced reduction in the maximal capacity to produce voluntary muscle force. When testing the isolated effects of moderate levels of dehydration (2-3%), most studies have found that it did not affect maximal muscle force (GREIWE et al., 1998; JUDELSON et al., 2007) or power production (HOFFMAN et al., 1995; WATSOM et al., 2005; JUDELSON Maet al., 2007). In controlled laboratory studies including prolonged exercise in the heat, dehydration has been shown to be accompanied by body temperature increases (GONZALEZ-ALONSO et al., 2008). The combination of dehydration and hyperthermia reduced running performance in the heat (CASA et al., 2010) and the production of muscle force (COSO et al., 2008), likely due to a failure in the central nervous system to drive the motoneurons (COSO et al., 2011). PETERSEN et al. (2007) found in eight elite marathon runners a 22% reduction in the capacity of the knee extensor muscles to produce force mainly related to central mechanisms. However, these authors did not relate the reduction of muscle performance with dehydration or hyperthermia.

Most marathon runners in the present investigation reduced their maximal production of power during a jump, indicating that leg muscle was fatigued after the marathon (Figure 2). In addition, they significantly reduced their body mass by 2.2 ± 1.2%. Although we did not measure body core temperature, which represents a limitation of this investigation, we consider that the subjects were hyperthermic during the post-race measurements since high post-race rectal temperatures (> 38 ºC) are consistently documented in marathon runners (CHEUVRONT & HAYMES, 2001). Nevertheless, there was no correlation between the change in body mass attained during the race and the change in leg muscle power production ($r = -0.08$; $P = 0.35$), at least in the levels found in this study. Thus, it seems that the hydration status was not the primary factor that determined muscle fatigue in the marathon runners. Nevertheless, these data do not question the importance of rehydrating during marathon races to avoid cardiovascular drift, hyperthermia and exercise-heat illnesses.

In addition to central factors, muscle fatigue may arise from peripheral changes at the level of the muscle. It has been reported that strenuous exercise can damage the muscle fibres (FRIDEM et al., 1983) producing the release of muscle proteins (mainly myoglobin) into the blood stream. Symptoms of exertional muscle damage are force loss, muscle soreness, pain and swelling which generally develop several hours after exercise, with peaks between 24 and 48 hours post exercise (CLARKSON & HUBAL, 2002). SCHIFF et al. (1978) investigated the myoglobin concentration of 44 runners completing a 99km ultra-distance race. They found that only six runners (13% of the sample) presented considerable levels of myoglobin in urine (a marker of muscle damage) after the race. However, they did not study if these six runners were the most fatigued after the marathon. Similarly, we have found a urinary myoglobin content higher than 10 $\mu g \cdot mL^{-1}$ in 9% of our sample. In addition, we have found that those runners with higher levels of power loss after the race were the ones with higher levels of urinary myoglobin (Figure 3). Interestingly, the runner with the highest fall in muscle power production (62%) was the one with the highest value of urinary myoglobin content (52.3 $\mu g \cdot mL^{-1}$). Thus, the drop in muscle performance during a marathon might be related to muscle fibre damage.

The presence of red blood cells in the urine (haematuria) is a clinical problem that indicates altered function of the kidney. However, haematuria is one of the most commonly found urine abnormalities after sports activity (ABARBANEL et al, 1990). MCINNIS et al. (1998) investigated the effects of different exercise protocols on post-exercise haematuria. They found weight-bearing exercise activities (running *vs* cycling) increased post-exercise haematuria and that exercise intensity was an increasing factor. Others authors have found that haematuria is present in 20 to 50% of marathon finishers (REID et al., 1987; GUR et al., 1994). In accordance with previous data,

we found that erythrocytes concentration increased from pre-race traces (0.4 ± 0.6 $U \cdot \mu L^{-1}$) to 23.2 ± 61.0 $U \cdot \mu L^{-1}$ after the marathon. In addition, the prevalence of haematuria increased from 1 to 34% after the race, with 6% of cases above 250 $U \cdot \mu L^{-1}$. These data suggest the necessity of obtaining an exercise history when haematuria is found in a patient.

In summary, the body mass change attained by amateur marathon runners in a warm environment was uneven. Most runners rehydrated according to fluid ingestion guidelines although there were 7.2% of subjects that reduced their pre-race body mass above 4%. To judge by our data, over-hydration was present in only 2% of the runners but body mass increases were close to 1% in all of them. The reduced capacity to generate power during a countermovement jump was correlated with the urine myoglobin concentration after the race, suggesting that muscle fatigue following the marathon is in some way associated with muscle fiber damage.

ACKNOWLEDGMENTS

The authors wish to thank the subjects for their invaluable contribution to the study. In addition, we are very grateful to the Elipse Iniciativas (the Organisation of the Madrid Marathon) for their contribution to the study.

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REFERENCES

1. ABARBANEL, J.; BENET, A. E. et al. (1990). "Sports hematuria." J Urol 143(5): 887-890.

2. ABIAN-VICEN, J.; DEL COSO, J. et al. (2012). "Analysis of dehydration and strength in elite badminton players." PLoS One 7(5): e37821.

3. EIS, L. Y.; WRIGHT-WHYTE, M. et al. (2012). "Drinking behaviors of elite male runners during marathon competition." Clin J Sport Med 22(3): 254-261.

4. BROWN, S. J.; CHILD, R. B. et al. (1996). "Changes in human skeletal muscle contractile function following stimulated eccentric exercise." Eur J Appl Physiol Occup Physiol 72(5-6): 515-521.

5. CASA, D. J. (1999). "Exercise in the Heat. II. Critical Concepts in Rehydration, Exertional Heat Illnesses, and Maximizing Athletic Performance." J Athl Train 34(3): 253-262.

6. CASA, D. J.; STEARNS, R. L. et al. (2010). "Influence of hydration on physiological function and performance during trail running in the heat." J Athl Train 45(2): 147-156.

7. CLARKSON, P. M. & HUBAL, M. J. (2002). "Exercise-induced muscle damage in humans." Am J Phys Med Rehabil 81(11 Suppl): S52-69.

8. CLARKSON, P. M.; KEARNS, A. K. et al. (2006). "Serum creatine kinase levels and renal function measures in exertional muscle damage." Med Sci Sports Exerc 38(4): 623-627.

9. CLARKSON, P. M. &. SAYERS, S. P (1999). "Etiology of exercise-induced muscle damage." Can J Appl Physiol 24(3): 234-248.

10. COSO, J. D.; ESTEVEZ, E. et al. (2008). "Anaerobic performance when rehydrating with water or commercially available sports drinks during prolonged exercise in the heat." Appl Physiol Nutr Metab 33(2): 290-298.

11. COSO, J. D.; HAMOUTI, N. et al. (2011). "Reproducibility of two electrical stimulation techniques to assess neuromuscular fatigue." Eur J Sport Sci 11(2): 95-103.

12. CHEUVRONT, S. N. & HAYMES, E. M (2001). "Thermoregulation and marathon running: biological and environmental influences." Sports Med 31(10): 743-762.

13. CHEUVRONT, S. N.; HAYMES, E. M. et al. (2002). "Comparison of sweat loss estimates for women during prolonged high-intensity running." Med Sci Sports Exerc 34(8): 1344-1350.

14. CHEUVRONT, S. N.; MONTAIN, S. J. et al. (2007). "Fluid replacement and performance during the marathon." Sports Med 37(4-5): 353-357.

15. FRIDEN, J.; SJOSTROM, M. et al. (1983). "Myofibrillar damage following intense eccentric exercise in man." Int J Sports Med 4(3): 170-176.

16. GANDEVIA, S. C. (2001). "Spinal and supraspinal factors in human muscle fatigue." Physiol Rev 81(4): 1725-1789.

17. GONZALEZ-ALONSO, J.; CRANDALL, C. G. et al. (2008). "The cardiovascular challenge of exercising in the heat." J Physiol 586(1): 45-53.

18. GREIWE, J. S.; STAFFEY, K. S. et al. (1998). "Effects of dehydration on isometric muscular strength and endurance." Med Sci Sports Exerc 30(2): 284-288.

19. GUR, H.; KUCUKOGLU, S. et al. (1994). "Effects of age, training background and duration of running on abnormal urinary findings after a half-marathon race." Br J Sports Med 28(1): 61-62.

20. HOFFMAN, J. R.; STAVSKY, H. et al. (1995). "The effect of water restriction on anaerobic power and vertical jumping height in basketball players." Int J Sports Med 16(4): 214-218.

21. JUDELSON, D. A.; MARESH, C. M. et al. (2007). "Effect of hydration state on strength, power, and resistance exercise performance." Med Sci Sports Exerc 39(10): 1817-1824.

22. KIRBY, T. J.; TRIPLETT, N. T.et al. (2011). "Effect of leucine supplementation on indices of muscle damage following drop jumps and resistance exercise." Amino Acids 42(5): 1987-1996.

23. MCINNIS, M. D.; NEWHOUSE, I. J. et al. (1998). "The effect of exercise intensity on hematuria in healthy male runners." Eur J Appl Physiol Occup Physiol 79(1): 99-105.

24. MEYER-BETZ, F. (1910). "Beobachtugen an einem eigenartigen mit muskellahmungen verbundenen fall von hamoglobinurie." Dtsc Arch Klin Med 101(1): 85-127.

25. MONTAIN, S. J. & COYLE, E. F. (1992). "Influence of graded dehydration on hyperthermia and cardiovascular drift during exercise." J Appl Physiol 73(4): 1340-1350.

26. MOON, J. R.; SMITH, A. E. et al. (2009). "Total body water changes after an exercise intervention tracked using bioimpedance spectroscopy: a deuterium oxide comparison." Clin Nutr 28(5): 516-525.

27. NOAKES, T. D. (2007). "Drinking guidelines for exercise: what evidence is there that athletes should drink "as much as tolerable", "to replace the weight lost during exercise" or "ad libitum"?" J Sports Sci 25(7): 781-796.

28. NOAKES, T. D. (2007). "Hydration in the marathon : using thirst to gauge safe fluid replacement." Sports Med 37(4-5): 463-466.

29. PASSE, D.; HORN M. et al. (2007). "Voluntary dehydration in runners despite favorable conditions for fluid intake." Int J Sport Nutr Exerc Metab 17(3): 284-295.

30. PETERSEN, K.; HANSEN, C. B. et al. (2007). "Muscle mechanical characteristics in fatigue and recovery from a marathon race in highly trained runners." Eur J Appl Physiol 101(3): 385-396.

31. RAMA, R.; IBANEZ, J. et al. (1994). "Hematological, electrolyte, and biochemical alterations after a 100-km run." Can J Appl Physiol 19(4): 411-420.

32. REID, R. I.; HOSKING, D. H. et al. (1987). "Haematuria following a marathon run: source and significance." Br J Urol 59(2): 133-136.

33. RODRIGUEZ, N. R.; DIMARCO, N. M. et al. (2009). "Position of the American Dietetic Association, Dietitians of Canada, and the American College of Sports Medicine: Nutrition and athletic performance." J Am Diet Assoc 109(3): 509-527.

34. SAWKA, M. N.; BURKE, L. M. et al. (2007). "American College of Sports Medicine position stand. Exercise and fluid replacement." Med Sci Sports Exerc 39(2): 377-390.

35. SCHIFF, H. B.; MACSEARRAIGH, E. T. et al. (1978). "Myoglobinuria, rhabdomyolysis and marathon running." Q J Med 47(188): 463-472.

36. SMITH, J. E.; GARBUTT, G. et al. (2004). "Effects of prolonged strenuous exercise (marathon running) on biochemical and haematological markers used in the investigation of patients in the emergency department." Br J Sports Med 38(3): 292-294.

37. WATSON, G.; JUDELSON, D. A. et al. (2005). "Influence of diuretic-induced dehydration on competitive sprint and power performance." Med Sci Sports Exerc 37(7): 1168-1174.