

Inflammatory profile and tissue injury in runners (5, 10, 15 km) and ultramarathon: IL-6, myoglobin

Perfil inflamatório e lesão tecidual em corredores (5, 10, 15 km) e ultramaratona: IL-6, mioglobina

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ABSTRACT

Introduction: Understanding the inflammatory responses and changes in muscle damage biomarkers induced by endurance exercise is crucial for optimizing training and recovery protocols. **Method:** This study analyzed interleukin-6 (IL-6) and myoglobin (MYO) levels in 75 recreational runners in Vitória-ES, across distances of 5, 10, 15 km, and a 12-hour ultramarathon (79.93 ± 28.65 km). The runners had average paces of 5.19 ± 1.22 min/km (5 km), 5.16 ± 0.57 min/km (10 km), 4.36 ± 0.12 min/km (15 km), and 10.91 ± 5.83 min/km (ultramarathon). Capillary blood samples were collected using micro EDTA tubes, with digital puncture and automatic lancets, and analyzed by point of care testing (POCT) technology. **Results:** 5 km, IL-6 decreased by 27.30% and MYO increased by 240.41%. 10 km, IL-6 decreased by 13.99% and MYO increased by 343.31%. 15 km, IL-6 decreased by 3.10% and MYO increased by 1062.61%. Ultramarathon IL-6: Pre: 7.66 ± 3.77 pg/ml, Mid-race: 48.55 ± 81.57 pg/ml (+ 533.68%), Post-race: 26.54 ± 20.82 pg/ml (-91.84% relative to pre-exercise). Eight days later: 4.07 ± 1.47 pg/ml (-46.86% relative to pre-exercise). Myoglobin: Pre: 22.42 ± 19.73 ng/ml, Mid-race: 314.19 ± 160.76 ng/ml (+ 1300.85%), Post-race: 423.07 ± 149.65 ng/ml (+1787.20% relative to pre-exercise). Eight days later: 40.50 ± 18.81 ng/ml (+ 80.70% relative to pre-exercise). **Conclusion:** The variability in responses reinforces the need for monitoring and individualized approaches, considering biopositive and bionegative adaptations resulting from biological individuality and physiological capacity.

Keywords: interleukin-6; myoglobin; running; inflammation; biomarkers; muscle fatigue.

RESUMO

Introdução: Compreender respostas inflamatórias e alterações nos biomarcadores de dano muscular provocadas pelo exercício de endurance é crucial para otimizar protocolos de treino e recuperação. **Método:** Este estudo analisou os níveis de interleucina-6 (IL-6) e mioglobina (MYO) em 75 corredores recreacionais em Vitória-ES, distâncias de 5, 10, 15 km e ultramaratona 12 h (79,93 ± 28,65 km). Os corredores apresentaram paces médios de 5,19 ± 1,22 min/km (5 km), 5,16 ± 0,57 min/km (10 km), 4,36 ± 0,12 min/km (15 km) e 10,91 ± 5,83 min/km (ultramaratona). As amostras de sangue capilar foram coletadas em micro tubos EDTA, com punção digital e lancetas automáticas, analisadas por tecnologia POCT (point of care testing). **Resultados:** 5 km IL-6: PRÉ 4,33 ± 2,28 pg/ml e PÓS: 3,16 ± 2,64 pg/ml, (-27,30%). Mioglobina: PRÉ: 22,39 ± 8,50 ng/ml e PÓS 63,11 ± 28,70 ng/ml, (+ 240,41%). 10 km IL-6: PRÉ: 4,78 ± 2,11 pg/ml PÓS: 4,17 ± 2,53 pg/ml, (-13,99%). Mioglobina: PRÉ: 30,43 ± 12,30 ng/ml e PÓS: 129,70 ± 45,60 ng/ml (+343,31%). 15 km IL-6: PRÉ: 5,99 ± 1,98 pg/ml. PÓS: 5,70 ± 2,45 pg/ml (-3,10%). Mioglobina: PRÉ: 28,91 ± 10,70 ng/ml. PÓS: 263,88 ± 85,50 ng/ml (+1062,61%). Ultramaratona IL-6: Pré: 7,66 ± 3,77 pg/ml Meio: 48,55 ± 81,57 pg/ml (+ 533,68%), Pós: 26,54 ± 20,82 pg/ml, (- 91,84%) em relação ao pré-exercício. Oito dias após: 4,07 ± 1,47 pg/ml (- 46,86%) em relação ao pré-exercício. Mioglobina: Pré: 22,42 ± 19,73 ng/ml, Meio da prova: 314,19 ± 160,76 ng/ml (+1300,85%), Pós: 423,07 ± 149,65 ng/ml, (+ 1787,20%) em relação ao pré-exercício. Oito dias após: 40,50 ± 18,81 ng/ml (+ 80,70%) em relação ao pré-exercício. **Conclusão:** A variabilidade nas respostas reforça a necessidade de monitoramento e abordagens individualizadas, considerando as adaptações biopositivas e bionegativas resultantes da individualidade biológica e lastro fisiológico.

Palavras-chave: interleucina-6; mioglobina; corrida; inflamação; biomarcadores; fadiga muscular.

Introduction

Long-distance running has emerged as a widely adopted practice in Brazil, especially in vibrant urban centers like the metropolitan region of Vitória-ES [1-3]. This phenomenon not only reflects a trend towards health and well-being but also provides a rich platform to investigate the complexities of physiological responses to exercise [3]. In 2021, Vitória was recognized as one of the “Brazilian Cities Friendly to Physical Activity” by PUC-PR, highlighting the local commitment to healthy practices and sustainable urban development [4].

Endurance exercise, while widely recognized for its cardiovascular health benefits and overall well-being [5,6], also induces an acute inflammatory response [7-10]. This response can result in exercise-induced muscle damage (EIMD), characterized by an increase in metabolic demand and the production of reactive oxygen species (ROS) [11,12]. These ROS have the potential to compromise muscle cell membrane integrity, resulting in the release of tissue biomarkers into the bloodstream [11].

In this context, two biomarkers stand out: interleukin-6 (IL-6) and myoglobin. IL-6, released by both muscles and the immune system during intense physical activity [14], serves as a central mediator of the inflammatory response [13,15,10,16-19]. Its release is a clear indicator of physical and inflammatory stress, essential for adapting and modulating the body's immune response to exercise [13,14,16-19]. Myoglobin, an essential muscle protein, is released into the bloodstream when cell damage occurs [20-22], serving as a direct marker of muscle injury and reflecting the extent of tissue damage induced by physical exertion [20-22].

Monitoring these biomarkers is crucial due to interindividual variability [23], influenced by factors such as age, training level, genetics, and nutrition [13]. This variability is especially important for recreational runners, as it significantly affects recovery and injury risk [2]. Understanding inflammatory and muscle damage response patterns in specific populations allows for the optimization of recovery strategies and exercise prescriptions, improving practitioners' quality of life and preventing long-term health complications [23].

This study aims to characterize IL-6 and myoglobin levels in recreational runners at various distances in the metropolitan region of Vitória-ES. Additionally, it seeks to correlate these responses with anthropometric and performance variables, highlighting the importance of monitoring these biomarkers in exercise management. By understanding these responses, we can develop more personalized approaches to recovery and injury prevention, promoting safer and more effective sports practice. This not only contributes to individual health but also advances scientific knowledge in the field of sports and physical exercise.

Methods

Study design

This study was conducted during 5 km, 10 km, 15 km, and ultramarathon events (12 hours duration, with an average distance of approximately 80 km) in the metropolitan area of Vitória-ES. The study has a longitudinal and observational design, without intervention, focusing on monitoring changes over time. There was no randomization of protocols or participants, characterizing it as a cohort study. The research was approved by the Ethics Committee of the University of Vila Velha (CAAE 78770017.0.0000.5064), and all participants signed the Informed Consent Form (ICF) before data collection.

Sample eligibility criteria

The sample included 75 recreational runners, distributed among the distances of 5 km, 10 km, 15 km, and ultramarathon (12-hour duration, average distance of approximately 80 km). Inclusion criteria were: (1) age over 18 years; (2) participation in at least one running event in the past year; (3) absence of acute musculoskeletal injuries. Exclusion criteria included: (1) presence of chronic inflammatory diseases or infections; (2) use of anti-inflammatory drugs seven days prior to collection; (3) pregnancy; (4) inability to participate in pre-exercise blood collection.

Ultramarathon eligibility criteria

Age: over 18 years; no participation in more than one ultramarathon that year; absence of acute musculoskeletal injuries; participation in at least one running event in the past year. Exclusions: presence of chronic inflammatory diseases or infections; use of anti-inflammatory drugs seven days prior to collection; pregnancy; inability to participate in pre-exercise blood collection.

Data collection

The table below presents the performance evaluated by running pace, in minutes per kilometer, using data from individual athletes' wearables (Global Positioning System - GPS), confirmed and/or adjusted by the official race results.

Table I - Performance Evaluated by Running Pace

Distance (km)	Number of runners	Average pace (min/km)
5 km	27	5.19 ± 1.22
10 km	18	5.16 ± 0.57
15 km	6	4.36 ± 0.12
Ultramarathon (79.93 ± 28.65)	24	10.91 ± 5.83

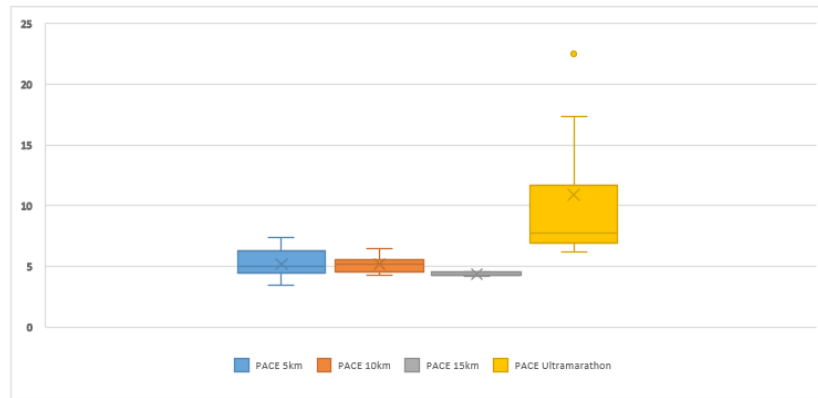


Figure 1 - Runner group summary

Blood sample collection and analysis

Capillary blood samples were collected in EDTA microtubes by finger lobe puncture, using G-Tech 28G automatic lancets, at two points: (1) pre-exercise, at rest, at least 30 minutes before the run; (2) immediately post-run, for the 5, 10, and 15 km groups. For the ultramarathon group, samples were collected at four points: (1) pre-exercise, at rest, at least 30 minutes before the run; (2) mid-race (approx. 6h into the race); (3) immediately post-race (12h post); and (4) eight days post-race. Samples were analyzed using the AFIAS-6, an automated fluorescence immunoassay point-of-care system, offering quick and precise biomarker identification.

Inflammatory biomarker determination

Levels of interleukin-6 (IL-6) for understanding inflammatory response status and myoglobin for understanding tissue (muscle) injury status were measured using the AFIAS-6, which combines the accessibility of point-of-care systems with the robustness of automated systems. This method offers fast and reliable results for biomarker evaluation.

Statistical Analysis

Descriptive analysis was performed with calculations of mean, standard deviation, minimum, and maximum for the biomarkers at pre and post-exercise moments. The percentage of variation was calculated using the formula:

$$\frac{(\text{Post-value} - \text{Pre-value})}{\text{Pre-value}} \times 100$$

Correlations between body weight and biomarker variation were tested using Pearson's correlation coefficient. All analyses were conducted using statistical software with a significance level of $p < 0.05$.

Results

The table below presents the mean, minimum, and maximum values of the biomarkers IL-6 and Myoglobin for the 5km runners group, before and after exercise, along with the observed percentage of variation.

Table II - Changes in Pre and Post-Exercise Biomarkers for 5km

Biomarker	Pre-exercise	Post-exercise	% Variation
IL-6 (pg/ml)	Mean: 4.33 ± 2.28	Mean: 3.16 ± 2.64	-27.30%
	Minimum: 1.05	Minimum: 0.50	
	Maximum: 8.67	Maximum: 7.90	
Myoglobin (ng/ml)	Mean: 22.39 ± 8.50	Mean: 63.11 ± 28.70	240.41%
	Minimum: 10.25	Minimum: 22.00	
	Maximum: 45.30	Maximum: 110.00	

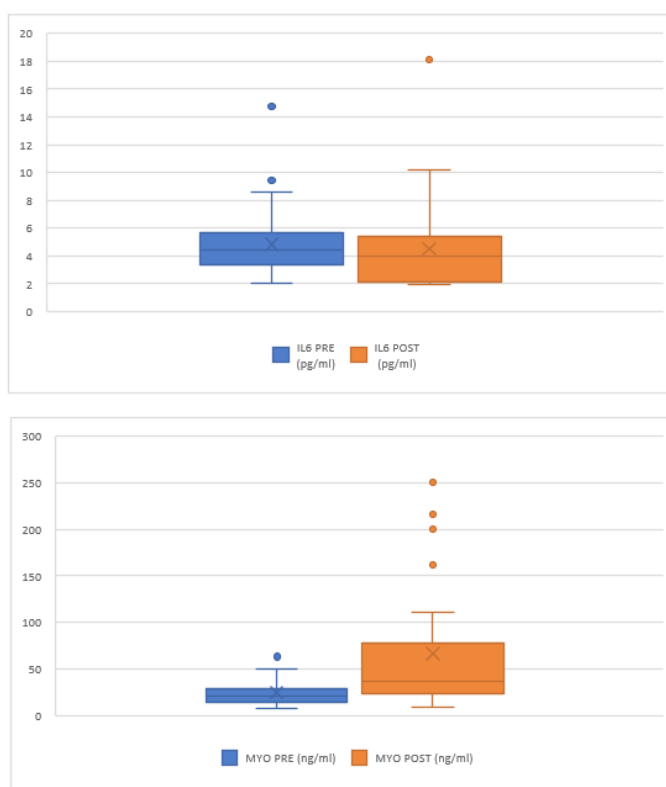
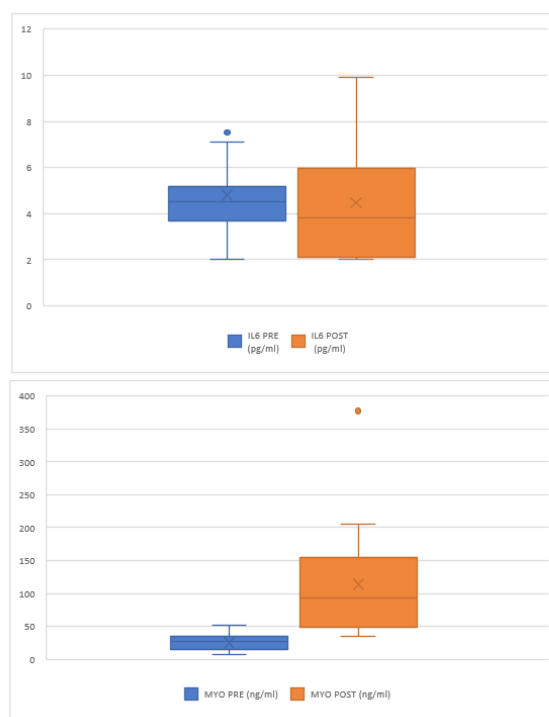


Figure 2 – Results 5 km

The table below presents the mean, minimum, and maximum values of the biomarkers IL-6 and Myoglobin for the 10km runners group, before and after exercise, along with the observed percentage of variation.

Table III - Changes in Pre and Post-Exercise Biomarkers for 10km

Biomarker	Pre-exercise	Post-exercise	% Variation
IL-6 (pg/ml)	Mean: 4.78 ± 2.11	Mean: 4.17 ± 2.53	-13.99%
	Minimum: 1.50	Minimum: 0.95	
	Máximo: 9.20	Máximo: 8.70	
Myoglobin (ng/ml)	Mean: 30.43 ± 12.30	Mean: 129.70 ± 45.60	343.31%
	Minimum: 15.50	Minimum: 50.00	
	Maximum: 60.00	Maximum: 200.00	

**Figure 3** – Results 10 km

The table below presents the mean, minimum, and maximum values of the biomarkers IL-6 and Myoglobin for the 15km runners group, before and after exercise, along with the observed percentage of variation.

Table IV - Alterações nos Biomarcadores Pré e Pós-Exercício 15km

Biomarker	Pre-exercise	Post-exercise	% Variation
IL-6 (pg/ml)	Mean: 5.99 ± 1.98	Mean: 5.70 ± 2.45	-3.10%
	Minimum: 3.50	Minimum: 2.50	
	Maximum: 8.50	Maximum: 9.00	
Myoglobin (ng/ml)	Mean: 28.91 ± 10.70	Mean: 263.88 ± 85.50	1062.61%
	Minimum: 18.00	Minimum: 150.00	
	Maximum: 55.00	Maximum: 400.00	

The table below presents the mean, minimum, and maximum values of the biomarkers IL-6 and Myoglobin for the ultramarathon runners group, before and after exercise, along with the observed percentage of variation.

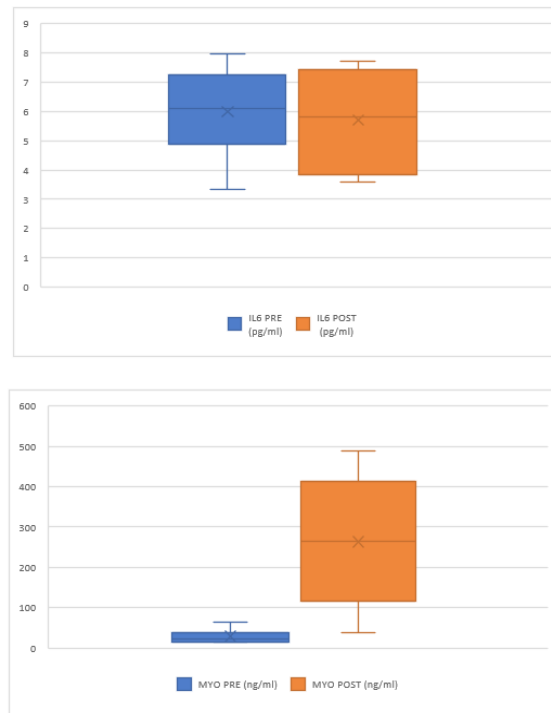


Figure 4 – Resultads 15 km

Table V - Changes in Pre and Post-Exercise Biomarkers – Ultramarathon

	Minimum	Mean	Maximum	
km	32	79.93 ± 28.65	116	
Pace (min/km)	22.5	10.91 ± 5.83	6.2	
Biomarker	Pre-exercise	During ½	Post-exercise	8 days post
IL-6 (pg/ml)	Mean: 7.66 ± 3.77	Mean: 48.55 ± 81.57	Mean: 26.54 ± 20.82	Mean: 4.07 ± 1.47
	Minimum: 3.43	Minimum: 6.84	Minimum: 2.39	Minimum: 3.04
	Maximum: 20.39	Maximum: 389.26	Maximum: 94.67	Maximum: 6.99
% variation	Pré-exercício	Durante ½	Pós-exercício	8 Days Post
	892.91 ± 1234.72	91.84 ± 41.58		555.37 ± 537.69
	Minimum: 122.37	Minimum: 10.01	Minimum: 104.15	Minimum: 122.37
Myoglobin (ng/ml)	Maximum: 5529.26	Maximum: 234.67	Maximum: 1883.88	Maximum: 5529.26
	Mean: 22.42 ± 19.73	Mean: 314.19 ± 160.76	Mean: 423.07 ± 149.65	Mean: 40.50 ± 18.81
	Minimum: 5.47	Minimum: 97.87	Minimum: 64.65	Minimum: 23.65
% Variation	Maximum: 83.02	Maximum: 500	Maximum: 500	Maximum: 78.90
	Pre-exercise	During ½	Post-exercise	8 Days Post
		2219.44 ± 1828.47		
% Variation		During ½	Post-exercise	8 Days Post
			85.75 ± 36.28	
			Post-exercise	8 Days Post
				1322.92 ± 710.82
	Minimum: 312.79	Minimum: 25.47		Minimum: 50.12
	Maximum: 7062.15	Maximum: 326.73		Maximum: 2114.16

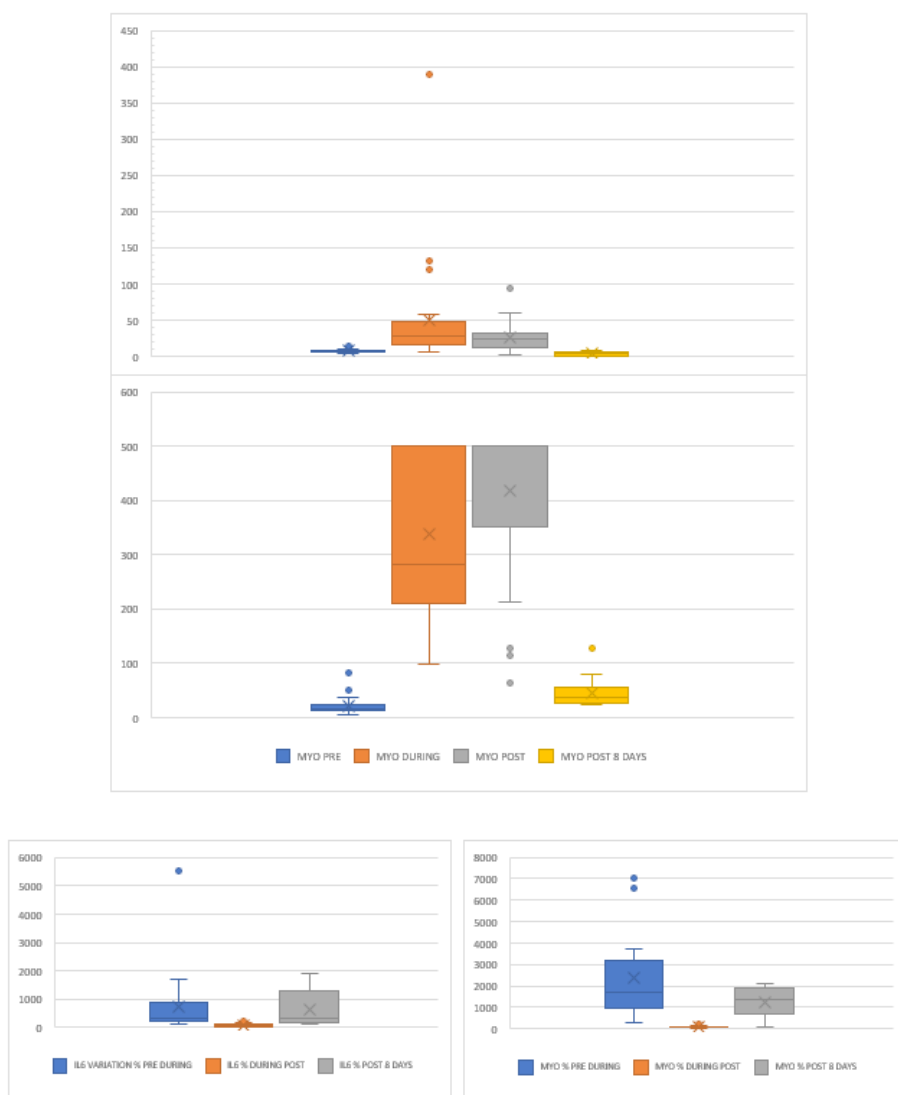


Figure 5 – Results ultramarathon

Correlations between pace and biomarker

The table below presents the correlation data between pace and biomarkers (IL6 and Myoglobin) for each group of runners.

Table VI - Correlações entre pace e variação de biomarcadores

Distance	Pace vs. IL-6	Pace vs. myoglobin
5 km	$r = 0.10$ ($p > 0.05$)	$r = 0.46$ ($p > 0.05$)
10 km	$r = 0.32$ ($p > 0.05$)	$r = 0.04$ ($p > 0.05$)
15 km	$r = 0.49$ ($p > 0.05$)	$r = 0.02$ ($p > 0.05$)
Ultramarathon	$r = 0.27$ ($p > 0.05$)	$r = 0.50$ ($p > 0.05$)

Discussion

Long-distance running, especially in ultramarathon events, offers a unique opportunity to explore the complexities of physiological responses to exercise, particularly in the urban context of Vitória-ES [2], a city recognized for its commitment to healthy practices [4]. The ultramarathon, involving 12-hour runs, presents significant challenges to the human body, highlighting the need to understand the inflammatory and muscle damage responses associated with such extreme exercise.

Endurance exercise, like ultramarathons, is widely recognized for its cardiovascular health benefits and overall well-being [5,6]. However, it also triggers an acute inflammatory response [7,8,10], which can result in exercise-induced muscle damage (EIMD) [11]. This phenomenon is characterized by increased metabolic demand and the production of reactive oxygen species (ROS) [11,12], which can compromise muscle cell membrane integrity and release tissue biomarkers into the bloodstream.

Two critical biomarkers in this context are interleukin-6 (IL-6) and myoglobin. During ultramarathons, IL-6 levels experience a significant increase, reflecting the intense inflammatory response and physical stress associated with these prolonged runs [10,14]. IL-6, released by both muscles and the immune system [15-17], acts as a central mediator of the inflammatory response [18,19], modulating the immune response to intense exercise. In contrast, myoglobin, a muscle protein [20,21], is released into the blood when cell damage occurs, serving as a direct marker of muscle injury [22]. During ultramarathons, myoglobin levels increase substantially, indicating the extent of tissue damage.

Monitoring the kinetics of these biomarkers is crucial due to interindividual variability [9], influenced by factors such as age, training level, genetics, and nutrition [13]. This variability is especially relevant for recreational runners participating in ultramarathons [2], as it significantly affects recovery and injury risk. Understanding inflammatory and muscle damage response patterns in ultramarathon events allows for the optimization of recovery strategies and exercise prescriptions, improving participants' quality of life and preventing long-term health complications [23].

This study aims to deepen the understanding of IL-6 and myoglobin responses in ultramarathon runners in the metropolitan region of Vitória-ES. Additionally, it seeks to correlate these responses with anthropometric and performance variables [3], underscoring the importance of monitoring these biomarkers in exercise management. Understanding these responses allows the development of more personalized approaches to recovery and injury prevention, promoting safer and more effective sports practice. This not only contributes to individual health but also advances scientific knowledge in the field of sports and physical exercise, providing valuable insights for coaches, athletes, and health professionals.

Analysis by running distance

5 km

IL-6 pre vs. post-levels: There was a decrease from 4.33 ± 2.28 pg/ml to 3.16 ± 2.64 pg/ml (-27.30%). This reduction suggests that in shorter runs, the inflammatory response may be minimal or recovery begins quickly after the run.

Myoglobin pre vs. post-levels: Increased from 22.39 ± 8.50 ng/ml to 63.11 ± 28.70 ng/ml (+240.41%), indicating some degree of muscle damage, but on a smaller scale compared to longer distances.

10 km

IL-6 pre vs. post-levels: Levels decreased from 4.78 ± 2.11 pg/ml to 4.17 ± 2.53 pg/ml (-13.99%). The slight decrease suggests a moderate inflammatory response that is quickly regulated.

Myoglobin pre vs. post-levels: Increased from 30.43 ± 12.30 ng/ml to 129.70 ± 45.60 ng/ml (+343.31%), showing a more pronounced increase in muscle damage compared to 5 km.

15 km

IL-6 pre vs. post-levels: Slight reduction from 5.99 ± 1.98 pg/ml to 5.70 ± 2.45 pg/ml (-3.10%). This indicates that the inflammatory response is more sustained but still controlled.

Myoglobin pre vs. post-levels: Rose from 28.91 ± 10.70 ng/ml to 263.88 ± 85.50 ng/ml (+1062.61%), indicating a substantial increase in muscle damage, which becomes more pronounced with increased distance.

Ultramarathon

IL-6 Levels: Pre vs. Mid: Increase from 7.66 ± 3.77 pg/ml to 48.55 ± 81.57 pg/ml (+533.68%), reflecting an intense inflammatory response.

Pre vs. Post: Reduction to 26.54 ± 20.82 pg/ml (-91.84% relative to pre) and further decrease to 4.07 ± 1.47 pg/ml eight days after (-46.86% relative to pre), indicating a prolonged recovery process.

Myoglobin pre vs. mid-levels: Increased from 22.42 ± 19.73 ng/ml to 314.19 ± 160.76 ng/ml (+1300.85%), showing a sharp increase in muscle damage.

Pre vs. Post: Increase to 423.07 ± 149.65 ng/ml (+1787.20%), with levels still elevated eight days later (40.50 ± 18.81 ng/ml, +80.70% relative to pre), suggesting that muscle recovery is more extended.

General discussion

The data from this study highlight a clear correlation between the distance covered and the intensity of physiological responses, specifically in terms of inflammation and muscle damage. As running distance increases, there is an escalation

in both the inflammatory response and muscle damage indicators, as evidenced by rising levels of interleukin-6 (IL-6) and myoglobin.

Responses in short-distance runs

In shorter runs, such as 5 km, inflammatory responses are more moderate, and recovery is fast. This may be due to shorter duration of intense physical exertion, which allows the body to better manage metabolic stress and tissue damage. Studies show that shorter-duration activities result in less pronounced inflammatory responses, facilitating more efficient recovery [13].

Responses in medium-distance runs

For 10 km and 15 km runs, there is a more noticeable increase in IL-6 and myoglobin levels. This increase suggests that, as distance and intensity of effort increase, the body faces more significant metabolic demand, resulting in a more robust inflammatory response and evident muscle damage [10].

Responses in ultramarathons

In ultramarathon events, the inflammatory response and muscle damage become significantly more pronounced. Prolonged running results in substantial production of reactive oxygen species (ROS), increasing oxidative stress and muscle damage. This type of extreme exercise requires more elaborate and prolonged recovery strategies [12].

Importance of individualized monitoring

Interindividual variability in physiological responses, influenced by factors such as age, training level, and genetics, underscores the need for personalized monitoring. The literature emphasizes the importance of adapting recovery and training strategies to athletes' individual needs, considering their unique characteristics and competition types [7].

Implications for training and recovery

Understanding the relationship between running distance and physiological response is crucial for developing effective training programs. Coaches and athletes can use this information to adjust training loads and implement recovery strategies that maximize performance and minimize injury risk. Additionally, this knowledge can inform exercise prescription and nutritional counseling, ensuring athletes are physically prepared to handle the challenges of long-distance running. In conclusion, this study not only emphasizes the importance of adapting recovery strategies to exercise distance and intensity but also highlights the need for individualized approaches, considering the complexity of the physiological responses involved.

Conclusion

Understanding these physiological dynamics allows for the development of more personalized approaches to recovery and injury prevention, promoting safer and more effective sports practice. Furthermore, precise biomarker monitoring provides valuable insights for performance optimization and injury risk reduction, contributing to significant advances in the field of sports and exercise science.

Conflicts of interest

The authors declare no conflicts of interest.

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Author contributions

Concept and design: Affonso HO; **Data collection:** Affonso HO, Souza MB; **Analysis and interpretation:** Affonso HO, **Manuscript writing:** Affonso HO, Souza MB, **Critical review:** Affonso HO

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