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Endurance Performance in Competitive Elite Female Athletes 18-25 Years Old with The HFF Genotype

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1. Abstract

1.1. Aim: Hereditary hemoglobinopathy can cause individuals to absorb too much iron from their diet. Higher tissue iron levels, below the threshold of toxicity, can enhance oxygen transport capacity and provide a competitive advantage. Single nucleotide polymorphisms (SNPs) in the homeostatic iron (HFE) regulatory gene have been shown to modulate iron metabolism and can be used to predict an individual's risk of hemoglobinopathy. Several studies have shown that the HFE genotype is associated with elite endurance athlete status; however, no studies have examined whether the HFE genotype of elite female athletes is associated with endurance performance.

1.2. Objective: The objective of this study was to determine if there was an association between HFE risk genotypes (rs1800562 and rs1799945) and endurance performance in the 8 km cycling time test as well as maximal oxygen uptake (VO2peak), an indicator of aerobic capacity.

1.3. Methods: Competitive female athletes (n = 60; 18-25 years) completed an 8 km cycling time trial. DNA was isolated from saliva and genotypicized for SNPs rs1800562 (C282Y) and rs1799945 (H63D) in HFE. Athletes were classified as low risk (n = 48) or medium/high risk (n = 12) based on their HFE genotype for both SNPs using an algorithm. ANCOVA was performed to compare outcome variables between both groups.

1.4. Results: People with medium or high risk genotypes were ~8% faster (1.3 minutes) than those with low risk genotypes (17.0 ± 0.8 vs 18.3 ± 0 ,3 minutes, P = 0.05). VO2peak was ~17% higher (7.9 mL • kg − 1.min − 1) in individuals with intermediate or high risk genotypes compared with those with low risk genotype (54.6 ± 3.2). Compared with 46.7 ± 1.0 mL • kg − 1.min − 1, P = 0.003).

1.5. Conclusion: This study shows that HFE risk genotypes are associated with improved endurance performance and increased VO-2peak in elite female athletes aged 18-25 years.

2. Introduction

Iron is a component of the storage protein hemoglobin (Hb), which transports oxygen and myoglobin, stores oxygen in active skeletal muscles, and facilitates transport to mitochondria. Iron is also an essential mineral found in many foods and also in dietary supplements.

Iron also enables erythropoiesis, the production of red blood cells (RBC). RBC supplies oxygen to all organs and tissues in the body including skeletal muscle and the heart [3]. Iron homeostasis is regulated by several genes, one of which is the human iron homeostasis (HFE) protein. HFE is a major unclassified histocompatibility protein located on the cell membrane that regulates intestinal iron absorption [15]. The HFE protein, encoded by the HFE gene, binds to transferrin receptor 2 (TFR2), which regulates hepcidin production. Hepcidin is a cyclic peptide hormone that inhibits iron absorption by binding to and degrading iron exporter ferroportin [15, 20]. The role of hepcidin is to regulate serum iron levels by preventing the release of iron from the duodenum into the bloodstream. This is an important function because too much iron in the blood can lead to iron overload and cause an increase in the release of free radicals, which can cause oxidative stress and muscle damage [15].

The common single nucleotide polymorphism (SNP) in HFE, 845G>A (rs180562), also known as C282Y, disrupts disulfide bond formation in the HFE protein, causing it to assemble intracellularly [15]. This combination prevents HFE from binding to TFR2, ultimately reducing hepcidin release [15]. Decreased hepcidin levels lead to ferroportin degradation, which facilitates the transport of iron from the duodenum into the bloodstream. This can disrupt the tightly controlled regulation of serum iron levels, leading to an excess of iron in the blood [15]. The "A" allele of the C282Y polymorphism is associated with excess iron storage, such that homozygous AA puts a person at increased risk of developing an iron overload known as hereditary hemoglobinopathy. HH) [22], [2]. The H63D polymorphism (rs1799945), H63D C>G, is another common SNP in HFE; however, its effect on iron status was not pronounced. This polymorphism still results in the generation of a stable complex with TFR2, but with a lower binding affinity. This also resulted in a decrease in hepcidin, but to a lesser extent than in the rs1800562 SNP [13]. The "G" allele of the H63D polymorphism is associated with excess iron stores, although to a lesser extent than the "A" allele of the C282Y polymorphism, and is associated with moderate risk of HH. Excess iron in the blood stream saturates transferrin iron-absorbing receptors, which can react with hydrogen peroxide or lipids and other reactive oxygen species [22].

Subsequently, the production of reactive oxygen species can lead to oxidative stress or tissue damage [15, 12]. C282Y has a greater penetration capacity than H63D; therefore, the C282Y polymorphism has a stronger effect on HH risk than the H63D variant.

HFE risk genotypes for iron overload are more common in competitive athletes [14, 10] reported that 41% of French elite athletes and 80% of medalists in European/international competitions had at least one risk variant in HFE (including rs1800562 and rs1799945) compared to 27% of the French population as a whole. [10] showed that 49.5% of athletes possessing an HFE SNP increased their risk of HH, compared with 33.5% of the general population. The elite athlete population includes individuals from a variety of sports, suggesting that HFE risk variants for iron overload confer a potential athletic performance advantage. After exercise-induced inflammation, hepcidin levels are upregulated to prevent iron absorption [20]. However, for athletes with moderate or high HFE risk variants, hepcidin release may not be upregulated, which would increase plasma iron bioavailability [14, 15, 20]. Higher serum iron concentrations may contribute to increased erythropoiesis because iron is required for hemoglobin production in RBC [7]. Increased RBC production and higher Hb levels may allow increased oxygen delivery to skeletal muscle, allowing for the maintenance of aerobic fitness, which is important for endurance athletes [20, 11]. The objective of this study was to determine whether the HFE genotype (rs1800562 and rs1799945) was associated with athletes' endurance performance as well as their maximal aerobic capacity.

3. Method

All subjects provided written consent and were informed that they may terminate participation at any time. Seventy competitive female athletes were selected from a variety of sports, including endurance type (e.g., triathlon, cycling), strength type (e.g. boxing, volleyball, weightlifting) and combined or mixed sports (eg, soccer, soccer, swimming). Athletes are required to train and/or compete for ≥8 hours • -1 week, for 9 out of 12 months per year for at least 3 years in their primary sport.

Eight athletes dropped out because of sports-related injuries, two because of school or work needs. The remaining 60 athletes had an average age of 18-25 years and a body mass of 61.0 ± 12.1 kg. Experimental design. Athletes completed four rounds, each ~100–130 minutes apart and approximately 1 week, in the exercise lab at the Science Center for High Performance Sports at Ho Chi Minh City University. Anthropometric measurements were collected and the athletes performed a maximal aerobic capacity (VO2peak) test and completed a questionnaire on athletic history and general health during the visit. their first. Saliva samples were also obtained for genotyping at the primary examination using the Oragene ON-500 kit according to standard procedure (DNA Genotek, Ottawa, Ontario, Canada) [16]. Athletes were asked to maintain regular sleeping and eating habits, avoid strenuous activity 48 hours prior to each visit, and abstain from caffeine 1 week prior to the first exam and for the remainder of the session. data collection (4 weeks total). To ensure dietary consistency, athletes were instructed to repeat the same meal they consumed prior to the first physical exam for subsequent visits. In tests 2–4, athletes were randomly assigned 0, 2 or 4 mg of caffeine per kg of body mass (mg • kg − 1).

Rating parameters. After receiving their randomly assigned dose of caffeine, the athletes completed a 25-minute questionnaire, followed by a 7-minute warm-up routine that began with light cycling. After completing the warm-up, the athletes performed four fitness tests, including vertical jump, hand run, Wingate, and 8 km (TT) cycling time trial.

Only 8 km TT cycling results are reported here. Maximum exercise test (VO2peak). Maximum aerobic capacity is measured through the VO2peak test. The test started at a working speed of 50 Won a braked and mechanically weighted cycle meter (Monark Ergomedic 839E; Monark Practice AB, Vansbro, Sweden), with a load increment of 50 W per minute for 2 min. first, then 25 W per minute thereafter until physical exhaustion. A portable metabolic system was used to measure gas exchange (Cortex Metamax 3B; CORTEX Biophysik GmbH, Leipzig, Germany). Maximum oxygen uptake (V˙O2peak) is defined as the highest 1-minute oxygen uptake value obtained during the test. The V˙O2peak power (W) is calculated by measuring the transmit power (W) at V˙O2peak. Final power The power is calculated using the output power (W) at voltage fatigue.

TT The 8 km TT exercise is the last of the four exercises that the athletes do first. Athletes begin cycling 8 km TT when blood lactate levels fall below 2.5 mmol•L-1 (after Wingate test), as measured by finger prick test and analyzed by Lactate Scout 4, from the previous Wingate test. An Ergomedic 839 E stationary bike was set at constant resistance or power and each subject cycled 8 km at the specified resistance (W). Resistance is set to 65% Wpower for all subjects based on calculations from the V˙O2peak test, or 65%-69% V˙O2peak. The on-board computer automatically controls the level of drag through the application of different braking forces on the belt. Speed is calculated based on pedal rhythm (rpm); Faster tempo will lead to faster speed. An 8 km long TT requires 1667 revolutions (6 m per revolution). Different cadences will result in different completion times for this test. Subjects could not see their time, speed, and heart rate but could see the distance traveled. The water has been performed ad libitum. Heart rate was monitored throughout the test using a heart rate monitor. Subjects determined their RPE using the Borg rating scale (rating scores from 6 [no exertion] to 20 [extremely difficult]) at 5 and 9 km.

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Table 1: Hemochromatosis risk classified based on HFE genotypes.

Hemochromatosis Risk	rs1799945	rs1800562
High	CC	AA
	GC	AA
	GG	AA
Medium	GC	AG
	GG	AG
	GG	GG
Low	CC	GG
	GC	GG
	CC	AG

The secondary outcome variable is VO2peak (mL • kg − 1.min − 1), where a larger value indicates better aerobic fitness and the variables adjusted for the type of sport included and % body fat.

ANCOVA was used to determine the effect of HFE risk groups, individual SNPs, and sports categories on V˙O2peak. If a significant effect was observed (P ≤ 0.05), post hoc analyzes using Tukey's HSD were performed. Since there was only one athlete in the high-risk group, athletes were stratified based on hemoglobin risk into two groups: medium/high risk or low risk.

4. Results

Subject characteristics. Of the 70 Athletes, 85.71% (n = 60) were characterized as low risk and 14.29% (n = 10) were considered medium/high risk. The descriptive characteristics of both risk groups are shown in (Table 2). Athletes in the intermediate or high risk group had a VO2peak measurement (mL kg-1.min − 1 and L • min. -1) significantly higher than athletes in the low-risk group. There were no significant differences between genotypes in terms of body mass, height, age, body fat percentage or percent distribution by sport type. The distribution by sport type of all participants was as follows: 37% endurance, 47% strength, and 16% mixed. For SNP rs1799945, 41 participants were CC, 15 were GC, and 4 were GG. For SNP rs1800562, 50 participants were GG, 9 were AG, and 1 was AA.

TT performing. (Figure 1) shows the average TT time of 8 km for all subjects (n = 60). There was a significant difference in TT achievement of 8 km between the low and moderate/high risk groups (P = 0.05). Those in the medium or high risk group outperformed those with the low risk genotype by ~8% (1.3 min) (17.0 ± 0.8 vs 18.3 ± 0.3 min, P = 0.05).

We then tested whether SNP rs179945 alone was associated with 8 km TT performance but found no difference between genotypes (P = 0.5). However, a significant association was observed between rs1800562 SNP and 8 km TT performance (P = 0.02). Post hoc analyzes showed that AA genotype outperformed GG genotype on cycling distance of 8 km TT by ~5 min (P=0.05). Effect of type of sport is significant on physical performance (P = 3.7 10−5); therefore, post-sport analyzes using Tukey's HSD were used to compare TT performance across sports categories. Post hoc analyzes showed that endurance and mixed athletes outperformed strength athletes (P=0.0006 and P=0.007, respectively).

Maximum oxygen absorption (VO2peak). (Figure 2) shows the maximum oxygen uptake, i.e. V˙O2peak, for all subjects (n = 100). There was a significant difference in V˙O2peak between the low and moderate or high risk groups (P = 0.003). Individuals in the intermediate or high risk group had higher VO2peak (54.6 ± 3.2 mL • kg − 1. min -1) than individuals in the low risk group (46.7 ± 1, 0 mL • kg − 1.min −1). We then tested whether SNP rs179945 was exclusively associated with VO2peak but found no difference between genotypes (P = 0.7). However, a significant difference in V˙O2peak was observed between the three genotypes (P = 0.001) of the rs1800562 variant. Post hoc analyzes showed that the AA genotype had a VO-2peak greater than ~19.4 mL • kg − 1.min − 1 compared with the GG genotype (P = 0.05). Those with the AG genotype had a larger V˙O2peak than those with the GG genotype of 8.58 mL • kg − 1.min − 1 (P = 0.01).

The effect of sport type was significant for VO2peak (P = 7.5 10−5). Post-hoc analyzes showed that endurance athletes and mixed athletes had a greater O2peak than strength athletes (P=0.0002 and P=0.004, respectively).

Table 2: Descriptive characteristics of participants by iron overload risk.

Low Iron Overload Risk Medium/High Iron Overload Risk			
Characteristics	n=60	n=10	P
Body massb (kg)	64.2 ± 8.2	64.3 ± 6.6	0.64
Height (cm)	172 ± 6.1	172 ± 6.1	0.82
Age (yr)	23.2 ± 4.1	25.1 ± 3.6	0.25
Body fat (%)	13.5 ± 4.8	12.3 ± 4.1	0.12
Sport type, n (%)			0.6
Endurance	22 (50)	4 (10)	
Power	28 (54)	5 (6)	
Mixed	10 (46)	1 (14)	

a P values were derived using ANOVA, or for sport type by using chi-square.
b Mean ± SD (all values).

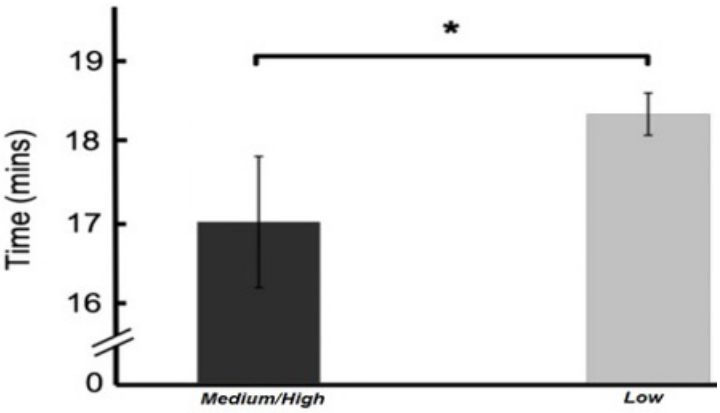

Figure 1: Average (mean ± SEM) 08-km cycling time by HFE risk genotype. *Those with the medium/high genotypes significantly outperformed (P = 0.05) those with the low-risk genotypes.

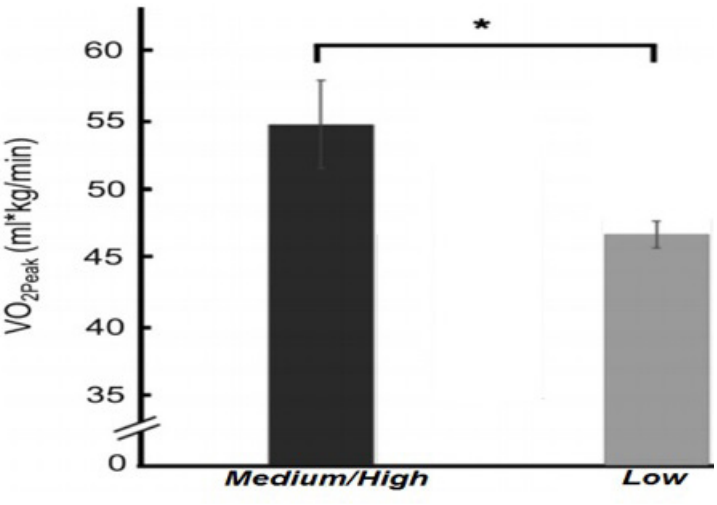

Figure 2: Average (mean ± SEM) V˙ O2peak by HFE risk genotype. *Those with the medium- or high-risk genotypes possess a significantly greater VO2peak (P = 0.003) compared with those with the low-risk genotypes.

5. Discussion

The results of our study show that the HFE risk genotype is associated with higher VO2peak. Specifically, our results show that athletes with moderate or high-risk HFE genotypes have approximately 17% higher VO2peaks than athletes with low-risk HFE genotypes. Examination of each SNP separately revealed that the effects were mainly driven by SNP C282Y (rs1800562). There were no significant differences in TT or VO2peak performance between genotypes of the H63D variant. This is inconsistent with a recent study that demonstrated the "G" allele of H63D to be associated with improved aerobic capacity [26].

The present study is the first to examine the association between HFE genotype and endurance performance in competitive female athletes. We also investigated the association between HFE genotype and aerobic capacity (VO2peak). Our results indicate that the HFE risk genotype is associated with improved endurance performance in the 8 km cycling TT. This is consistent with previous studies that have shown that iron overload risk genotypes are more common in elite endurance athletes than in the general population [10]. Notably, a recent meta-analysis report of 586 athletes of different ethnicities corroborated a higher prevalence of H63D polymorphisms in endurance athletes than in the general population, regardless of ethnicity. a person's ethnicity [26]. However, the meta-analysis only considered the effect of the allele of the H63D genotype [26]. The present study is the first to examine the association between an individual's risk of iron overload, as determined by the compound allele effect of the HFE genotypes C282Y and H63D, and endurance performance. This may be because the risk variant of C282Y has a greater penetrability than the risky variant of H63D [2]. It is also possible that the link between H63D and aerobic capacity has only been observed in higher-level competitive athletes, such as Olympic athletes [26].

Endurance athletes and mixed athletes outperform strength athletes on TT and have greater aerobic capacity. This suggests that endurance athletes perform better due to more training in this area than in other types of sports; however, a significant association between HFE genotype and 8 km TT performance as well as V˙O2peak was still present after controlling for sport type. Our findings are consistent with an important role of iron metabolism in endurance performance [1]. The main function of iron is to facilitate oxygen transport in the RBC and tissues via Hb [29]. Some studies show that exercise can stimulate red blood cell production, which reduces red blood cell count by age one [18, 19]. This will eventually increase a person's metabolic activity as the amount of young RBCs increases [18]. 2, 3-Diphosphoglycerate (2, 3-DPG) is a glycolysis intermediate produced in RBC. Increased exercise-induced metabolic activity may promote long-term elevation of the allergen Hb 2,3-DPG [18, 24]. Increased levels of 2,3-DPG reduce Hb-O2 affinity, promoting oxygen transport and delivery in the lungs and other tissues around the body [5]. In addition to Hb-O2 affinity, oxygen transport capacity is affected by the volume of Hb in a person's blood.

Athletes are at a lower risk of having iron levels than the general population because of increased training and competition demands [21], exacerbation of iron loss through excessive sweating, loss of iron excessive blood in the gastrointestinal tract and urine (from impact, jostling of organs), and the rapid breakdown of exercise-induced RBCs [25]. Endurance athletes are at higher risk than athletes from other sports [25, 28], likely due to increased hemolysis from impact to the leg among other factors. Iron deficiency can negatively affect athletic performance by reducing oxygen delivery to skeletal muscle, lowering blood pH, and rapidly depleting muscle glycogen stores [27]. Normal iron levels also allow the maintenance of redox balance in muscle and mitochondrial energy production, both of which are important for athletic performance [8]. One study suggested that endurance athletes are likely to have lower-than-normal Hb levels because of low iron levels, likely due to foot hemolysis [30]. Therefore, athletes are likely to consume iron supplements as an adjunct to improve maximal oxygen uptake [12, 19]. However, this can worsen athlete performance because excess iron can lead to increased oxidative stress, including muscle tissue damage [23]. An increased amount of Hb results in an increased amount of oxygen being transported to the tissues [18], which has been linked to improved athletic performance [6]. A close relationship exists between total Hbmass and maximum oxygen uptake (VO2max) [24]. Oxygen carrying capacity, relative to total Hbmass [18], is associated with different outcomes in endurance performance [18]. Increased blood Hb levels are associated with improved oxygen transport and, by extension, a person's maximal aerobic capacity [6]. Thus, improved oxygen uptake and aerobic capacity could provide a potential performance advantage for athletes by improving oxygen delivery to the muscles.

The risk variants C282Y and H63D can significantly reduce binding affinity for TFR2, which may downregulate hepcidin release leading to increased blood iron levels [22]. Iron concentrations above the

upper limit of normal may offer a potential performance advantage because of improved oxygen transport through hematological parameters such as Hb [12, 4]. The higher bioavailability of serum iron may lead to increased erythropoiesis that may increase the athlete's oxygen carrying capacity and maximal oxygen uptake due to elevated Hb [15]. Furthermore, increased erythropoiesis may also improve athletes' recovery between high-intensity interval exercise and muscle regeneration by reducing muscle fatigue [14]. Increased Hb is associated with HFE risk variant genotypes, which may explain the potential physiological difference compared with those without the risk variant [4].

The results of this study suggest that athletes may benefit from regularly monitoring their iron status and considering supplementation to optimize iron stores under expert guidance. nutritionist or other health professionals [15]. When monitoring and optimizing iron status, athletes, coaches, and their healthcare providers should keep their HFE genotypes in mind. Collectively, our results also demonstrate that the moderate/high risk of HH as determined by an individual's HFE genotype (rs1800562 and rs1799945) is associated with better endurance performance. However, the effect of HFE risk genotype is unknown on other performance measures, such as anaerobic strength-based exercise patterns.

Despite the potential to improve athletic performance in people with HFE risk variants, some studies have suggested otherwise [11, 17]. One study found that female adolescents with an H63D risk variant (n = 7) had lower aerobic capacity than those without a risk variant (n = 6) [17]. However, there are some limitations, such as the small sample size and the different sport modalities being evaluated, that may affect these results. Another study determined that the H63D risk variant did not predict performance at the 2008 Kona Ironman championship triathlon [11]. However, performance can be affected by many uncontrolled variables, including ambient temperature, pre-competition nutrition, the presence of overtraining syndrome, and familiarity with the sport. racing distances. Some limitations include that this study population included only competitive female athletes, so future trials will test whether HFE risk variants predict endurance and fitness performance. Rhythm in female and female recreational activities and female athletes compete or not. Another limitation is the small number of subjects with a rare genotype of each SNP that is associated with moderate or high risk.

6. Conclusion

In summary, we found that individuals with moderate or high-risk HFE genotypes (rs1800562 and rs1799945) outperformed those with low-risk genotypes in the 8-km cycling TT. Furthermore, people in the intermediate or high risk groups had a larger VO2peak than those at low HH risk. The results of our study highlight the importance of monitoring and optimizing the iron status of 18-25-year-old female athletes. This study was funded by the Sports Science Research Institute of Ho Chi Minh City, Vietnam National Research Foundation. The results of this study are not endorsed by the University Ho Chi Minh City of Sports. Results are presented clearly, honestly and without fabricating, falsifying or inappropriately manipulating data.

References

1. Abbaspour N, Hurrell R, Kelishadi R. Review on iron and its importance for human health. J Res Med Sci Off J Isfahan Univ Med Sci. 2014; 19: 164–74.
2. Allen KJ, Gurrin LC, Constantine CC. Iron-overload–related disease in HFE hereditary hemochromatosis. N Engl J Med. 2008; 358: 221–30.
3. Anker SD, Comin Colet J, Filippatos G. Ferric carboxymaltose in patients with heart failure and iron deficiency. N Engl J Med. 2009; 361: 2436–48.
4. Astle WJ, Elding H, Jiang T. The allelic landscape of human blood cell trait variation and links to common complex disease. Cell. 2016; 167: 1415–29.e19.
5. Bauer C. Antagonistic influence of CO2 and 2,3 diphosphoglycerate on the Bohr effect of human haemoglobin. Life Sci. 1969; 8: 1041–6.
6. Berglund B, Hemmingson P. Effect of reinfusion of autologous blood on exercise performance in cross-country skiers. Int J Sports Med. 1987; 8: 231–3.
7. Brutsaert TD, Hernandez-Cordero S, Rivera J, Viola T, Hughes G, Haas JD. Iron supplementation improves progressive fatigue resistance during dynamic knee extensor exercise in iron-depleted, nonanemic women. Am J Clin Nutr. 2003; 77: 441–8.
8. Buratti P, Gammella E, Rybinska I, Cairo G, Recalcati S. Recent advances in iron metabolism: relevance for health, exercise, and performance. Med Sci Sports Exerc. 2015; 47: 1596–604.
9. Calbet JAL, Lundby C, Koskolou M, Boushel R. Importance of hemoglobin concentration to exercise: acute manipulations. Respir Physiol Neurobiol. 2006; 151: 132–40.
10. Chicharro JL. Mutations in the hereditary haemochromatosis gene HFE in professional endurance athletes. Br J Sports Med. 2004; 38: 418–21.
11. Grealy R, Herruer J, Smith CLE, Hiller D, Haseler LJ, Griffiths LR. Evaluation of a 7-gene genetic profile for athletic endurance phenotype in ironman championship triathletes. Roemer K, editor. Plos one. 2015; 10: e0145171.
12. Guest NS, Horne J, Vanderhout SM, El-Sohemy A. Sport nutrigenomics: personalized nutrition for athletic performance. Front Nutr. 2019; 6: 8.
13. Hanson EH. HFE gene and hereditary hemochromatosis: a HuGE review. Am J Epidemiol. 2001; 154: 193–206.
14. Hermine O, Dine G, Genty V. Eighty percent of French sport winners in Olympic, World and Europeans competitions have mutations in the hemochromatosis HFE gene. Biochimie. 2015; 119: 1–5.
15. Hollerer I, Bachmann A, Muckenthaler MU. Pathophysiological consequences and benefits of HFE mutations: 20 years of research. Haematologica. 2017; 102: 809–17.

16. Josse AR, Da Costa LA, Campos H, El-Sohemy A. Associations between polymorphisms in the AHR and CYP1A1-CYP1A2 gene regions and habitual caffeine consumption. Am J Clin Nutr. 2012; 96: 665–71.

17. Luszczyk M, Kaczorowska-Hac B, Milosz E, et al. Reduction of skeletal muscle power in adolescent males carrying H63D mutation in the HFE gene. Biomed Res Int. 2017; 2017: 1–7.

18. Mairbäurl H. Red blood cells in sports: effects of exercise and training on oxygen supply by red blood cells. Front Physiol. 2013; 4–332.

19. Marengo-Rowe AJ. Structure–function relations of human hemoglobins. Bayl Univ Med Cent Proc. 2006; 19: 239–45.

20. McKay AKA, Pyne DB, Burke LM, Peeling P. Iron metabolism: interactions with energy and carbohydrate availability. Nutrients. 2020; 12: 3692.

21. Parks RB, Hetzel SJ, Brooks MA. Iron deficiency and anemia among collegiate athletes: a retrospective chart review. Med Sci Sports Exerc. 2017; 49: 1711–5.

22. Porto G, Brissot P, Swinkels DW. EMQN best practice guidelines for the molecular genetic diagnosis of hereditary hemochromatosis (HH). Eur J Hum Genet. 2016; 24: 479–95.

23. Recalcati S, Minotti G, Cairo G. Iron regulatory proteins: from molecular mechanisms to drug development. Antioxid Redox Signal. 2010; 13: 1593–616.

24. Schmidt W, Prommer N. Impact of alterations in total hemoglobin mass on V˙ O2max. Exerc Sport Sci Rev. 2010; 38: 68–75.

25. Sekulic D, Tahiraj E, Maric D, Olujic D, Bianco A, Zaletel P et al. What drives athletes toward dietary supplement use: objective knowledge or self-perceived competence? Cross-sectional analysis of professional team-sport players from Southeastern Europe during the competitive season. J Int Soc Sports Nutr. 2019; 16: 25.

26. Semenova EA, Miyamoto-Mikami E, Akimov EB. The association of HFE gene H63D polymorphism with endurance athlete status and aerobic capacity: novel findings and a meta-analysis. Eur J Appl Physiol. 2020; 120: 665–73.

27. Sim M, Garvican-Lewis LA, Cox GR. Iron considerations for the athlete: a narrative review. Eur J Appl Physiol. 2019; 119: 1463–78.

28. Sinclair LM, Hinton PS. Prevalence of iron deficiency with and without anemia in recreationally active men and women. J Am Diet Assoc. 2005; 105: 975–8.

29. Volpe SL. Iron and athletic performance. ACSMs Health Fit J. 2010; 14: 31–3.

30. Watts E. Athletes' anaemia. A review of possible causes and guidelines on investigation. Br J Sports Med. 1989; 23: 81–3.